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PROCEEDINGS
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Vol. 46 No. 11 November 1953

CONTENTS

Whole Proceedings Page

Section of Dermatology

April 16, 1953
CASES 901–905

May 21, 1953
CASES 906–908

Section of Radiology

The Last Decade and the Next: An Appraisal.—President's Address by CONSTANCE A. P. WOOD, M.A., M.R.C.P., F.F.R. 909

Section of General Practice

DISCUSSION: VAGINAL DISCHARGE AS SEEN IN GENERAL PRACTICE 915

Section of Anæsthetics

Some Electroencephalographic Changes Associated with Induced Vascular Hypotension.—P. R. BROMAGE, M.B., D.A., F.F.A.R.C.S. 919

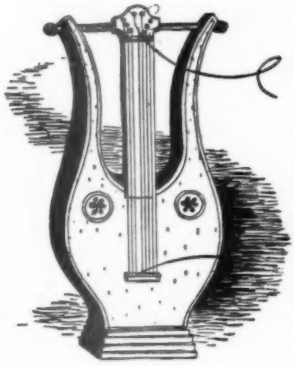
The Depression of Respiration by the Opiates and Its Antagonism by Nalorphine.—R. I. BODMAN, M.B., D.A... 923

Section of the History of Medicine

A Historical Note on the Simple Dementing Form of Schizophrenia.—JOSEPH ZELMANOWITS, M.D., D.P.M... 931

Jan Evangelista Purkyně—Czech Scientist and Patriot (1787–1869).—HENRY J. JOHN, M.D., F.A.C.P. 933

Continued overleaf



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CONTENTS (*continued*)

	Whole Proceedings Page
Section of Laryngology	
DISCUSSION ON HIATUS HERNIA AND ŒSOPHAGITIS [*Abridged*]	941
Section of Obstetrics and Gynæcology	
April 24, 1953	
DISCUSSION ON LESIONS OF THE INTESTINE AND OF THE URINARY TRACT RESEMBLING DISEASE OF THE FEMALE GENITAL TRACT	947
May 22, 1953	
Film and List of Specimens Shown	956
Section of Psychiatry	
February 10, 1953	
On Ageing.—E. E. KRAPF, M.D., F.R.F.P.S.	957
June 9, 1953	
DISCUSSION ON THE SURGERY OF TEMPORAL LOBE EPILEPSY	965
Section of Physical Medicine	
October 8, 1952	
A Study of Spinal Osteoporosis.—President's Address by DONALD WILSON, M.B., M.R.C.P.	977
April 8, 1953	
DISCUSSION ON THE PRESENT STATE OF PHYSICAL MEDICINE IN THE COUNTRIES OF EUROPE ..	981
May 16, 1953	
MEETING HELD AT COURTLANDS HOSPITAL, WEST WORTHING, SUSSEX	
Intractable Œdema of the Leg [*Abstract*].—CHARLES L. HEANLEY, F.R.C.S., M.R.C.P.	985
Rheumatoid Arthritis from the Point of View of a General Physician.—W. A. BOURNE, M.D.	986
Books Received for Review. Books Recently Presented and Placed in the Society's Library	990

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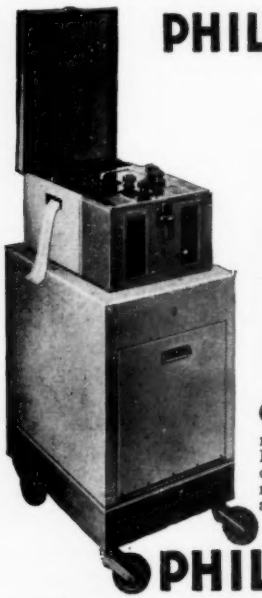

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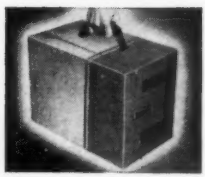

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Section of Dermatology

President—G. B. DOWLING, M.D., F.R.C.P.

[*April* 16, 1953]

Purpuric Pigmented Lichenoid Dermatitis.—H. W. BARBER, F.R.C.P., and H. HABER, M.D

M. B., aged 28, consulted one of us (H. W. B.) 24.3.53 on the advice of Dr. M. A. Shellim of Calcutta.

History.—He was in Burma from August 1949 until September 1951. In March 1951 the present eruption appeared on his left calf and persisted until his return to England where it disappeared within a month.

He went to Germany, and in April 1952 during a spell of hot weather the eruption relapsed and spread but almost cleared again during the ensuing cooler weather. In December 1952 he was sent to Calcutta and there was a further relapse which persisted with extension during a six-week stay in Chittagong.

Dr. Shellim suggested tentatively the diagnosis of the purpuric pigmented lichenoid dermatosis of Gougerot and Blum.

The patient arrived in England only a few days before I saw him, and already the eruption showed signs of involution. *He has never taken mepacrine.*

On examination (24.3.53): There was a widespread lichenoid pigmented eruption involving the feet, legs, thighs, buttocks and back. The clinical appearances resembled those of Gougerot and Blum's dermatosis. Blood pressure normal. Urine: morning and evening specimens rather concentrated (sp. gr. 1028) but normal apart from excess of indican. Teeth good. No buccal lesions.

The histopathological report (H. H.) is as follows:

"Two biopsies were performed:

"(1) *From a yellow tinted area.* The epidermis does not show any diagnostic features. There is a perivascular œdematous round-cell infiltration of the upper and middle network demonstrable. Stain for hæmosiderin negative.

"(2) *From a whole papule.* The papule is of epidermal origin. It consists of a parakeratotic scale containing many polymorphs as in psoriasis. The stratum granulosum is missing and the rete shows slight atrophy. There is a perivascular œdematous round-cell infiltration and arterioles are widely dilated and some engorged. Stain for hæmosiderin negative."

On examination (16.4.53).—The eruption has faded considerably, leaving staining similar to that seen in Schamberg's disease. The lichenoid papules have flattened. There are still definitely purpuric lesions on the dorsal surfaces of the feet.

POSTSCRIPT (11.6.53).—The patient reports that the eruption has almost entirely faded, apart from some staining.—H. W. B.

Dr. B. Phillips: The case appears very similar to those which were quite common in Normandy during the war and were known as "khaki dermatitis". Is there any possibility of this being exogenous? The starting-point seems to be capillary fragility.

Dr. R. T. Brain: I suggest that parapsoriasis is a possible diagnosis.

Dr. J. B. Sneddon: One case of the kind was shown at Liverpool last year by Dr. G. W. Bamber—a purpuric macular eruption. A suggested diagnosis was parapsoriasis.

REFERENCE

BAMBER, G. W. (1953) *Brit. J. Derm.*, **65**, 183.

Dr. H. W. Barber: I had considered the possibility of khaki dermatitis but the history of the eruption would ·em to exclude this diagnosis. With regard to parapsoriasis I agree with Civatte that pityriasis lichenoides ·uta vel chronica (parapsoriasis en gouttes) should be considered as entirely distinct from parapsoriasis ·i plaques and parapsoriasis lichenoides (parakeratosis variegata), but the eruption in this case does not, to ·y mind, resemble any of these, and in none have I observed the striking effect of temperature that is so ·pparent in my patient.

Toxic Capillaritis.—K. D. Crow, M.R.C.P.

Mr. F. W., aged 47.

Six months ago an eruption of brownish-red, pinhead, purpuric puncta appeared firstly on the right ankle and then on the left. Since that time it has gradually extended from the ankles to the tops of the thighs, round the umbilicus and on the axillary folds, antecubital fossæ and sides of the trunk until the whole of both legs and thighs as well as the other areas mentioned are densely clustered with the pinhead lesions which are scattered diffusely or aggregated in small groups or larger sheets. Below the knees many of the lesions are slightly raised and there is a fine, diffuse scaling in these areas.

Some considerable areas of the disease have cleared on the legs below the knees leaving a rather diffuse, brownish discoloration but in most areas the lesions are unchanged or slowly extending. During the last few weeks he has had considerable irritation but states that it has been spasmodic in nature and appears to be confined to the older lesions.

With the exception of a few tablets of sod. amytal taken just before the eruption first appeared he has taken no drugs of any sort. He had had no new articles of clothing but a suit was cleaned just before the onset. His diet is full and varied.

Investigations.—Bleeding time 1 min. 15 sec.; coagulation time 6 min. 30 sec.; platelets 190,000; R.B.C. 5,300,000; Hb 104%.

Test doses of sod. amytal and carbromal were without effect on the eruption.

Hess' test caused an exaggeration of existing purpuric lesions below the tourniquet, but no fresh lesions appeared.

Patch tests to propylene glycol extracts of material from all his suits, D.D.T. and a detergent were negative.

Discussion.—Doucas and Kapetanakis, in 1953, observed 177 cases of a condition exactly resembling this one but were unable to reach any definite conclusions as to the ætiology. The duration of the disease varied from a few months to two years. In a number of their patients, scaling together with small lichenoid papules was observed on the lower limbs and similar lesions have recently appeared in the present patient. This fact has led many American authors to believe that this condition and the one described by Gougerot as pigmented purpuric lichenoid dermatosis may well be identical.

Although the clinical picture was somewhat different, the prominence of purpuric lesions in the cases of khaki-shirt dermatitis described by Hodgson and Hellier in 1946 raises the interesting question of whether chemicals used in the processing of textiles may not, in fact, be responsible for some of these eruptions.

Postscript (3.6.53).—Most of the eruption has now disappeared but some of the lesions remain on the legs. Hess' test was again carried out on three further occasions at intervals of a few weeks and the results were unchanged, purpuric puncta appearing only in the site of pre-existing lesions. On a fourth occasion, however, when the eruption on the arms had disappeared, the test was still mildly positive but it was not then possible to say definitely whether the purpuric puncta arose in the site of previous lesions or not.—K. D. C.

REFERENCES

Doucas, C., and Kapetanakis, J. (1953) *Dermatologica*, **106**, 86.
Hodgson, G. A., and Hellier, F. F. (1946) *J. R. Army Med. Corps.*, **87**, 110.

Dr. R. D. Sweet: I have known such eruptions occur as a result of the washing of underclothing in a detergent.

Dr. D. E. Oakley: I have had a precisely similar case occurring in a man who worked in an experimental laboratory. He had his first eruption after he had been engaged in the laboratory for about nine months. I tried patch tests with a number of the chemicals he used (organic solvents of the trichlorethylene group) but got negative results. He left that research, however, and the condition cleared up, but three weeks ago he appeared again with a similar eruption and he tells me he has gone back to his previous research.

Dr. G. A. Beck: This patient told me that his eruption started on the legs above his socks. It is still confined to, or at least most severe in, those areas in closest contact with his trousers. I have just spoken to his dry cleaners and they tell me that a new "retexturing" process was introduced to their routine cleaning technique about a year ago.

It may be that the onset of his eruption soon after an accident was occasioned by the consequent need to wear a clean suit after it and that his various exacerbations can also be related to other occasions when he has worn suits fresh from the cleaners. I suggest that Dr. Crow pursues his enquiries along these lines.

Dr. A. Yorke: There may be more than one factor concerned in this reaction. I remember a very similar case in which the patient had an exacerbation immediately after the removal of some infected teeth and this slowly subsided. It had almost completely disappeared when the patient went away, to return about two or three years later with exactly the same picture. I went into the history of the patient very carefully and the doctor attending her said that she had been taking drugs of the Carbromal group. Thus it seems that in these patients one may get a cutaneous pattern reflecting two factors.

Dr. G. A. Hodgson: This case shows remarkable capillary fragility similar to that seen in textile dermatitis from Army shirts. How far this fragility, continued for a very long time, may account for the eruption I cannot say. I have seen one case which continued for as long as four years after the man had been retired from the Army. He still had the capillary fragility then. I think we must be dealing with an endogenous toxin.

Dr. I. B. Sneddon: I cannot agree that in these cases of textile dermatitis there is always a positive capillary fragility. About half of them, in my experience, *show such a factor*. In some cases this finding varies; one week a case may show a positive capillary fragility and the following week this has disappeared.

Lichen Spinulosus.—D. I. WILLIAMS, F.R.C.P. (Referred by HOWARD ELDER, M.D.).

S. H., aged 17 months.

History.—He is the only child of healthy parents; his progress has been normal except for the condition of the skin. It is thought that some "spots" which appeared on his nose in the first weeks of his life were the same as those now present; these early lesions were washed in olive oil and disappeared. At the age of 3 months he was vaccinated and around the vaccination site spiny spots developed. Many more similar lesions have since appeared in several sites, including the scalp. He was seen at King's College Hospital when he was 9 months old; since that time there has been no change except in the scalp lesions where the spiny nature of the papules has become less obvious and the involved areas have become diffusely pink.

Examination.—The eruption consists of papules about the size of a pinhead, red, conical and containing in their centre a horny spine, projecting about one-sixteenth of an inch. When the hand is passed over the affected region it imparts to it the sensation of a nutmeg-grater; this epidermic plug can be picked out, leaving a depression in the papule. There is little or no itching and the eruption gives but trifling inconvenience except from the discomfort produced by the horny spines catching in the clothing.

The papules are densely crowded into patches, often quite large and irregular in outline; there are striking lesions around the right knee and on the left arm. There are red areas on the scalp, of varying sizes, where there are tiny papules to be seen but where the previously marked spines are not obvious. It would not be right to say that there is any atrophy of the skin in these areas at present but the hair will not grow therein and I fear that it never will.

Permission for a biopsy has been sought but not yet with success.

Large doses of vitamin A have been given by mouth and in an ointment without the least effect on the eruption.

I suggest that this condition is an entity which is not often seen: I certainly have never seen it before. This is different from those cases of lichen planus with follicular lesions, particularly on the scalp which sometimes proceed to atrophy with a pseudo-pelade-like clinical appearance. The description of this case is quoted almost verbatim from Radcliffe Crocker's textbook (Diseases of the Skin. London, 1903): I am sure we should reserve the term lichen spinulosus, as he did, for this rare condition and call the Graham Little type, follicular lichen planus.

Dr. L. Forman: The usual course of this condition is that the follicles atrophy and there is a residual permanent atrophic alopecia. I know of no treatment which would favourably modify the course of the alopecia.

Dr. R. T. Brain: Has ringworm been considered?

Dr. Williams: I have not looked for ringworm. I will certainly do so but I do not think for a moment that it exists.

POSTSCRIPT.—Examination of hairs under the microscope and by Wood's light showed no evidence of ringworm.—D. I. W.

Lichen Spinulosus with Cicatricial Alopecia.—P. J. HARE, M.R.C.P.

A. B., student, aged 23.

For about a year the patient has noticed an eruption on the trunk. The affected areas itch a little when she gets hot. She recently noticed a patch of baldness on the scalp, but cannot recall any itching in that region. Her general health has been excellent. Eleven years ago she had malaria in Kenya, and she thinks she was treated with mepacrine. Last year she was preparing for her "Finals" at University (Arts) and at times felt run down and agitated. She was given a tonic containing iron and strychnine which she states she took for the better part of that year.

Physical examination.—Oral mucosa normal.

On the vertex there is a discoid area 2 cm. in diameter in which there is complete alopecia. The area is brownish red in colour and shows marked plugging of follicles (Fig. 1).

On the thorax there are fairly well-defined areas of crowded brown papules, some of which are domed and shiny, others acuminate with central dark brown spines. These areas occur over the clavicles, on the right breast and over the upper portion of the back (Fig. 2).

The rest of the skin appears normal.

Histology.—The lesion on the scalp (Fig. 4). shows pronounced plugging of the follicular ostia and a general hyperkeratosis. The epidermis is thin. In the dermis there is fibrosis, an infiltrate of lymphocytes and plasma cells and numerous clumps of melanin. The section is regrettably superficial, but as far as can be seen there is no trace of the deeper parts of the follicles or sebaceous glands.

FIG. 1.—Lesion on the scalp showing loss of hair and marked plugging of follicles.

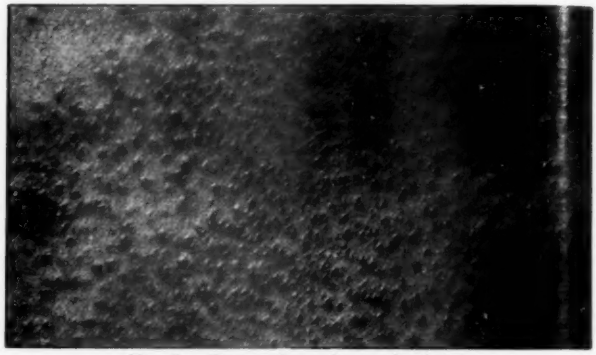

FIG. 2.—Group of papules on the thorax.

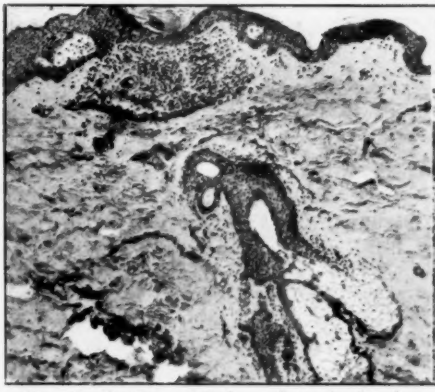

FIG. 3.—Section of lesion of trunk showing sharply defined patch of infiltrate at the upper end of a hair follicle.

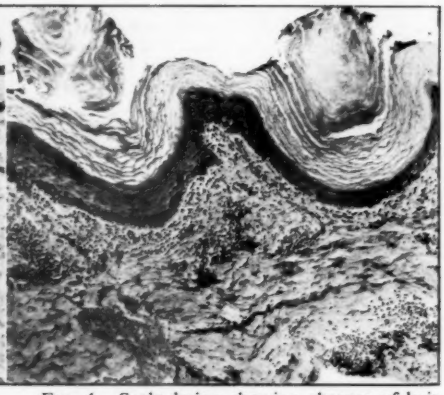

FIG. 4.—Scalp lesion showing absence of hair follicles, marked hyperkeratosis and rather diffuse infiltrate.

The section from the right breast (Fig. 3) shows a sharply demarcated area of infiltration around the upper end of a hair follicle, with lymphocytes, endothelial cells and a few giant cells of foreign body type. Over this the granular layer is increased and there is a little hyperkeratosis. The basal layer shows hydropic degeneration and dropping down of pigment.

Unilateral Spider Nævi of Pregnancy.—STEPHEN GOLD, M.D.

Mrs. V. G., aged 27, is nine months pregnant. This is her first pregnancy and she has been admitted to hospital owing to an antepartum hæmorrhage. In the second month of pregnancy she noticed "red blotches" on her left hand and arm. These have not greatly increased but the right hand remains completely free. There has been no injury to the left arm.

On examination.—Multiple "spider nævi" are present on the dorsum of the left hand, less on the palmar surface, wrist and forearm. The right upper limb, face, neck, upper trunk and buccal mucosa are free. There is no evidence of Raynaud attacks, vascular disease or scleroderma. She has suffered from chilblains in the past and has noticed that both arms are occasionally rather cold. Both palms show an equal degree of erythema.

General examination reveals no abnormality. Routine blood tests show normal findings.

Discussion.—I have seen one other similar case in a woman who broke her arm, while it was encased in plaster she realized that she was pregnant. On removal of the plaster there were multiple "spiders" over the plastered area. My patient to-day gives no history of trauma. It is reported (Bean *et al.*, 1949) that the majority of pregnant women reveal these vascular marks. They disappear soon after delivery and often recur in subsequent pregnancies. I have found no other report of a unilateral distribution such as is present in this case.

REFERENCE

BEAN, W. B., COGSWELL, R., DEXTER, M., and EMBICK, J. F. (1949) *Surg. Gynec. Obstet.*, **88**, 739.

Dr. L. Forman: "Spider nævi" occur very frequently in association with pregnancy. In one patient whom I showed here in 1934 (*Proc. R. Soc. Med.*, **27**, 723) the early sign of pregnancy was the development of large numbers of spider nævi on the face and chest; she had been pregnant twelve times, her first child was still living, but the other pregnancies ended in stillbirths. Spider nævi have been reported with carcinoma of the bronchus and particularly in association with oat-celled carcinoma. Spider nævi are known to be associated with liver disorders; Dr. William Bean (1942) produced "spider nævi in 2 out of 3 chronic alcohol addicts, and palmar erythema in 1, following therapy with potent œstrogens".

REFERENCE

BEAN, W. (1942) *Amer. J. med. Sci.*, **204**, 251.

Familial Hyperidrosis.—J. L. FRANKLIN, M.D.

Mr. R. R., aged 39.

This man has recently come from India for an opinion regarding his very severe hyperidrosis. He finds his hands and feet tend to pour sweat throughout the day and ease up only at night. His underclothing especially in relation to the axillæ and centre of abdomen becomes saturated.

The patient has a clear insight into the condition in that he realizes it is emotional to a large degree, but he also claims that it is hereditary and that both his parents who were first cousins, were affected by the condition.

He finds he gets some relief from taking Bellergal and wishes to now whether it is safe to continue with this and also requests advice regarding the value of sympathectomy in this condition.

The condition is so severe that in a few minutes a small pool of sweat forms on the floor beneath him if he does not continually mop his hands with his handkerchief.

Dr. Malcolm Tottie (Sweden): I have seen a case of familial hyperidrosis in a patient who was very unhappy over his condition. He was quite unable to control it and used 24 handkerchiefs a day. He was sent to a surgeon who carried out sympathectomy and this had a very good effect. Three years later the patient was quite happy and could stand up in big meetings without pouring out a fountain of water.

The President: Professor Keele has shown that the sweat glands in these patients are no more numerous or active than in individuals with comparatively dry skins, but they are very readily stimulated into violent activity by emotional stimuli. It has been suggested that such patients may benefit from psychiatric treatment. Whether this is so or not I cannot say, but as our Swedish visitor has remarked sympathectomy can be relied on to cure the condition, and though there may be some degree of relapse in the course of time it would not be as severe as at present. There is, however, a danger in sympathectomy if all four quarters are treated, since profuse and constant sweating on other parts of the body may follow.

The following cases were also shown:

Case for Diagnosis. ? Morphœic Atrophy of Subcutaneous Tissue.—Dr. MICHAEL FEIWEL.

Lichen Sclerosus.—Dr. L. FORMAN.

Dermatitis Artefacta.—Dr. L. FORMAN.

Pretibial Callosities.—Dr. J. S. PEGUM.

Two Cases of *Trichophyton rubrum* Infection.—Dr. C. D. CALNAN.

Diabetic Xanthoma.—Dr. H. BLACK (for Dr. G. B. MITCHELL-HEGGS).

Lupus Erythematosus Treated with Mepacrine.—Dr. I. A. MAGNUS (for Dr. L. FORMAN).

Squamous Epithelioma of Leg.—Dr. D. ANDERSON.

Nævus of Palm.—Dr. A. JARRETT (for Dr. P. J. HARE).

(These cases may be published later in the *British Journal of Dermatology*.)

[*May* 21, 1953]

Dermatofibrosarcoma Protuberans.—E. WADDINGTON, M.D., M.R.C.P.

CASE FIRST SHOWN AT MEETING ON FEBRUARY 19, 1953

Mrs. B. B., aged 38, has had a number of hard lumps on the abdomen for over twenty years. They caused her no discomfort until fourteen months ago, when one of the lumps began to increase in size and became tender on pressure.

On examination.—The lesion consists of an irregularly shaped plaque about the size of the palm of the hand, situated on the left side of the abdomen. The plaque is light brown in colour and freely movable with the skin. Arising from the surface there are numerous tumours; one of these involves the umbilicus and is the size of a golf ball. It is bluish red in colour and there are numerous telangiectases on the surface. (This lesion has increased in size during the last year.) (Fig. 1.)

There are also many cellular nævi, both pigmented and non-pigmented, on the face, neck and shoulders.

Biopsy report (Dr. I. W. Whimster).—A neurofibroma.

Comment.—Although some authors have suggested that this condition originates in nerve tissue, no histological proof of this has been offered, and it is generally considered to be a well-differentiated fibrosarcoma of low-grade malignancy.

The main reason for showing this patient is that the biopsy clearly shows that this is a neurofibroma

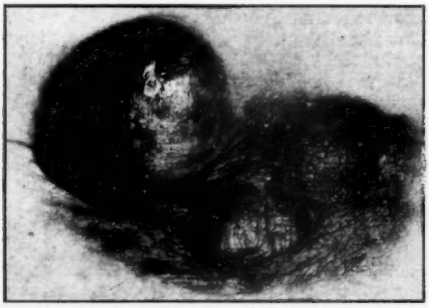

FIG. 1.—The lesion showing the pale-brown plaque and raised pink nodules.

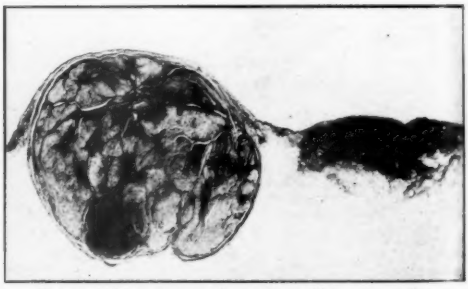

FIG. 2.—Low-power view of a section across the whole lesion (Van Gieson).

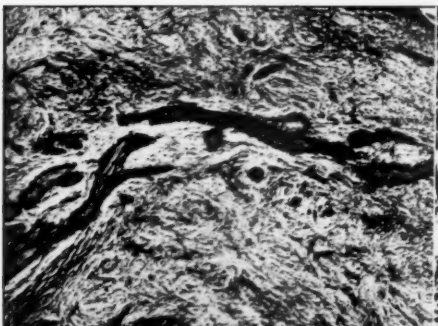

FIG. 3.—High-power view of part of the large lump showing laminated fibrous tissue continuous with the sheaths of nerves (Van Gieson).

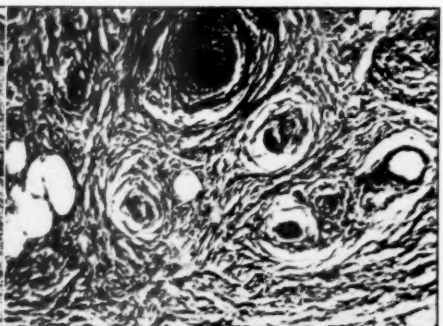

FIG. 4.—High-power view of the extreme edge of the plaque showing laminated fibrosis continuous with the sheaths of several small nerves near the base of a hair follicle (Van Gieson).

and the presence of multiple pigmented nævi on the face and limbs lends support to the view that dermatofibrosarcoma protuberans is closely related to von Recklinghausen's neurofibromatosis.

Dr. I. W. Whimster: Dr. Waddington's case seems to me to be an example of Paget's recurrent fibroid tumour (Paget, J., 1870, Lectures on Surgical Pathology, 3rd Ed.) and I recommend his description of the condition to all those interested. The natural history and histology of these lesions suggests that they represent diffuse, locally progressive neurofibrosis. They are accompanied, or often preceded, by pigmentation such as occurs in von Recklinghausen's disease and one case I saw recently complained of paræsthesiæ in the pigmented area prior to the onset of lumpiness. Examination of sections taken from the extreme periphery of these lesions shows fibrous overgrowth along the course of the nerves in the dermis. In the central lumpy parts of the lesions the fibrous overgrowth is so great that though its arrangement is characteristic of neural fibrous tissue its association with nerve fibres cannot easily be demonstrated. The recurrence of these lumps is, I think, attributable to the fact that the peripheral spreading part, which may extend widely, is invisible clinically and therefore is not often excised. At present we have only a small biopsy fragment from Dr. Waddington's case, and though it shows the characteristic laminated structure of neural fibrous tissue it is too small to permit demonstration of its nervous origin. The lesion will be excised and I hope at a later date to be able to demonstrate its neurofibromatous nature.

Continued (21.5.53):

Dr. I. W. Whimster: The lesion has now been excised widely and section across it shows quite clearly the origin of the fibrous tissue from nerve sheaths, both in the main lump and in the adjacent plaque (Figs. 2, 3 and 4).

The President: Have other cases presented evidence of neurofibromatous tissue?

Dr. Whimster: Every case of dermatofibrosarcoma protuberans that I have examined histologically has looked to me neurofibromatous.

Dr. H. Haber: I have examined several cases of dermatofibrosarcoma protuberans. The histology was always characteristic; it consisted of a very dense cellular infiltration of slender spindle-shaped cells arranged in rows and whorls. The whole picture resembled that of a cellular fibroma. The histology shown here by Dr. Whimster looks slightly different to me and I agree with Dr. Whimster that this is neurofibroma. I have the impression that there are cases of true neurofibroma which may simulate clinically dermatofibrosarcoma protuberans.

Epithelial Nævus.—R. J. CAIRNS, M.R.C.P.

A male, aged 14 years, is living in an orphanage and has had this skin trouble for as long as he can remember. No family history is available.

On examination.—The whole of the face and ears are erythematous and scaly. The border of the eruption is well defined and there are several outlying islands on the upper part of the neck and in the hairy part of the scalp. The hair, teeth and nails are normal.

On the extensor surfaces of the hands and forearms there is a similar erythemato-squamous eruption with well-defined follicular keratosis over the dorsal surfaces of the proximal phalanges and about the wrist. This erythro-keratosis is sharply marginated. The trunk is normal apart from slightly scaly lesions over the buttocks. The patches are well marked on the legs, particularly on the front of the knees and on the ankles. On the backs of the hands and knees there is a certain amount of secondary eczematization. The palms and soles are unaffected.

General examination is normal apart from a left external rectus palsy.

Investigations.—Blood count normal. Chest X-ray N.A.D. Mantoux negative 1 : 1,000.

Biopsy.—There is hyperkeratosis of the basket-weave type, moderate acanthosis and mild dermal cellular infiltration surrounding the blood vessels.

Comment.—Gans and Kochs (1951) described cases of this type. They emphasize that they should be distinguished from the congenital palmar and plantar keratoses and from congenital ichthyosiform erythrodermia. It appears usually in the first six months of life and progresses in a symmetrical fashion to affect particularly the dorsum of the hands, feet, knees and elbows. The palms and soles are characteristically free.

I feel that this present case must be a nævoid keratosis simulating to a certain extent both pityriasis rubra pilaris and the erythrokeratosis of Gans and Kochs.

REFERENCE

GANS, O., and KOCHS, A. G. (1951) *Hautarzt*, **2**, 389.

Dr. P. A. J. Smith: May I suggest that this is pityriasis rubra pilaris and that we do not know what it is, or how to treat it. If it is not pityriasis rubra pilaris we still do not know what it is or how to treat it.

Acute Lichen Planus—Treated with ACTH.—R. H. MEARA, M.R.C.P. (for G. B. DOWLING, M.D.).

M. K., male, aged 35.

History.—At the beginning of February 1953 he developed a widespread itching eruption. When first seen on February 18 the eruption consisted of violaceous, flat-topped, shiny papules widespread over the body, sparing only the palms, soles and scalp. There was considerable involvement of the buccal mucosa, tongue and lips. He was treated as an out-patient for a few weeks with no improvement and was then admitted to hospital on March 24. At that time he was complaining of severe itching and burning of the skin. After two weeks with no improvement, treatment with ACTH was started. One pint of normal saline containing 25 mg. of ACTH was given over a period of eight hours every day for eleven days. The symptoms of itching and burning disappeared within two days and within three days there was considerable improvement in the condition of the skin. At the end of the first week the lichen planus papules had resolved leaving intense brown pigmentation and the buccal lesions had healed. ACTH treatment was discontinued on April 28, and since then no further symptoms or lesions have developed.

On examination.—There are large irregular areas of deep brown pigmentation. No other lesions are present on the skin and the buccal mucosa is normal.

Comment.—This case has been presented because of the striking response of the patient to this hormone therapy.

Addendum (10.7.53).—The patient was seen again to-day and shows no evidence of relapse. The pigmented areas have faded considerably.

The President: We treated the patient with ACTH because of the severity of the symptoms. Dr. Whitfield at one time advocated lumbar puncture to provide relief from the intense itching of very acute widespread lichen planus. We expected an immediate response, but also some degree of relapse when the treatment was stopped. However, no relapse has followed. I do not, however, suppose that ACTH would have the least effect on chronic lichen planus, especially warty lesions on the legs.

The following cases were also shown:

Case for Diagnosis: Unilateral Orbital Pigmentation.—Dr. HENRY SEMON.

Light Sensitive Epidermolysis Bullosa.—Dr. BERNARD C. TATE.

Multiple Epitheliomatosis.—Dr. S. P. HALL-SMITH.

Angioma Serpiginosum.—Dr. E. LIPMAN COHEN.

Ichthyosis Vulgaris with Hyperkeratosis.—Dr. R. H. MARTEN (for Dr. F. R. BETTLEY).

Favus, Mother and Child.—Dr. R. H. MEARA (for Dr. G. B. DOWLING).

Macular Atrophy.—Dr. I. S. HODGSON-JONES and Dr. C. H. NICHOL.

(These cases may be published later in the *British Journal of Dermatology*.)

Section of Radiology

President—CONSTANCE A. P. WOOD, M.A., M.R.C.P., F.F.R.

[*April* 17, 1953]

The Last Decade and the Next: An Appraisal

PRESIDENT'S ADDRESS

By CONSTANCE A. P. WOOD, M.A., M.R.C.P., F.F.R.

Director, Radiotherapeutic Research Unit, Medical Research Council, Hammersmith Hospital

By tracing the developments which have taken place in radiotherapy in the last one or two decades, I shall try to make some assessment of what has already been achieved and what promise is held by the future.

One of the first needs of the radiotherapist was to establish some means by which he could measure the dose of radiation delivered to the patient. The roentgen unit which related the dose to the energy distributed by the radiation beam in the patient's body was established as the unit of measure in 1928. Improved apparatus for the absolute measurement of the roentgen made it possible in 1937 to adapt this unit for radium gamma rays as well as X-rays. The roentgen made possible a quantitative approach to the problems of dosimetry. Compared with the methods of trial and error which characterized X-ray therapy in the nineteen-twenties, the decade 1930 to 1940 stands out pre-eminently as one in which X-ray and gamma ray dosimetry was applied to the practical problems of radiotherapy.

Much work was done during this period to increase our knowledge of the dosage distribution in an X-ray beam as it passes through the patient. The large number of physical measurements required were made easier by a vast improvement in equipment specially designed for this purpose, such as mass-produced condenser ionization chambers and the use of remote control dose meters for exploring the beams. These devices have greatly improved the accuracy and the speed with which measurements can be made.

This increased knowledge of dose distribution has led to very great advances in the technique of treatment. The aim of all these techniques is to ensure that the whole tumour receives an adequate dose of radiation with minimum damage to surrounding structures. Much effort has gone into the planning of treatment and choice of fields for each individual patient. Wedge-shaped filters of wood and other materials have been introduced into the X-ray beam to make it stronger on one side than the other and so obtain a distribution suitable for particular sites. A study has been made of the way in which radiation beams combine together to give a complex dose distribution, and it is now possible to obtain a three-dimensional picture of the dosage distribution throughout the whole of the treated area. Many devices have been made for accurately directing the beam of radiation and for ensuring precise repetition of the treatment. The subject has been turned from an art into a science.

But the fact remains that, however carefully the planning is done, there is no way of improving the distribution beyond a certain point set by the properties of the X-ray beam itself. Faced with this daily problem of the necessity of a good dose distribution, it was inevitable that there should have been the greatest interest by those practising radiotherapy in the use of very high voltage X-rays. In my own Unit, in which we were carrying out an investigation into the value of radium beam therapy, the rapidly falling depth dose from such apparatus kept this problem constantly before us. It should first be said that it was impracticable to develop the conventional type of X-ray apparatus for a tension of several million volts. It was not simply a matter of cost. New technical ideas were needed before such X-ray apparatus became a practical possibility.

In 1938 the Medical Research Council granted a request we made to build a 2 million volt van der Graaff generator in order to obtain a better dose distribution within the patient than was possible with the 10-gramme radium beam apparatus which we were using for clinical work at that time. Van der Graaff machines did not become commercially available until many years later. The construction of this high voltage generator progressed very slowly during the war years and, by the time it was completed in 1944, work in the U.S.A. on super-voltage X-ray machines had resulted in the construction of a betatron producing X-rays at a much higher voltage than 2 MeV. We decided, therefore, to wait for apparatus having all the technical advances which could be foreseen before starting a trial of super-voltage therapy. For this and also for an even more important reason, to which I will refer later, we decided not to use our 2 MeV generator in 1944 for the treatment of patients, as was originally intended, but to use it as a source of radiation for radiobiological studies. Serious consideration was given by members of the Unit at this time to obtaining a betatron and adapting it for clinical use. It became apparent that many difficulties were encountered in the operation of the betatron and in 1945 the possibility of designing a linear accelerator became evident.

There was a sudden surge of interest in the decade 1940/1950 in the production and use of higher voltages and physicists and engineers developed the specialized techniques that were needed. As often happens, several ideas originated simultaneously in different parts of the world and these have resulted in the production of a variety of supervoltage X-ray machines. The arrival of the betatron, the synchrotron and the linear accelerator is in itself a full and fascinating story. They were first built for nuclear physics, but measurements of the high-voltage X-rays produced by them showed that they could offer much to the radiotherapist. Our knowledge of the physical characteristics of the higher energy radiations was rapidly enlarged when in 1943 depth dose curves for 4, 10 and 20 million volt X-rays were published. It was evident that radiation in this energy range gave a vastly improved dose distribution in the treatment of all but superficial tumours. This improvement made possible the treatment of even the most deeply seated tumours without any skin reaction.

A very lively interest was taken in these developments and it was hoped that these large and expensive machines could soon be brought into hospitals to give the much-needed improvement in treatment technique. The needs of a nuclear physicist, however, for a laboratory machine in which a certain amount of temperament is excusable are very different from those of a radiotherapist working to a carefully planned schedule of treatment.

Very soon the variety of machines became so wide that it was a matter of some difficulty to choose between them. Among the first in the field was the compact 2 MeV van der Graaff machine, developed far beyond its state in 1939. It is now commercially available from the U.S.A. in a form suitable for clinical use, and three of these machines are installed in hospitals in this country. Two 30 MeV synchrotrons financed by the M.R.C. have also been installed in this country. Unless some means can be found, however, of increasing their low output they are not very suitable for the treatment of any large number of cases. Since 1945 we had taken a keen interest in the possibility of using the new techniques for accelerating electrons and we collaborated closely with other groups in this country then interested in these ideas. Some two years later the 3·5 MeV travelling wave linear accelerator was brought into operation by the A.E.R.E. group working at T.R.E. Malvern. The successful operation of this machine at a high X-ray intensity at once made possible the development of a machine for clinical use, and this project was supported by the M.R.C. It has been the experience in many parts of the world that from the time a machine is working satisfactorily in the laboratory about four years' work is necessary to re-build it as a clinical machine ready for installation in a hospital. This is about the time taken with the M.R.C. linear accelerator, which has recently been completed and installed. It is a fixed machine but the X-ray beam can be angulated through 120°, and to obtain a vertical movement for positioning the patient the whole floor of the treatment room can be moved up and down over a distance of 5 feet. It is suspended from the ceiling, leaving the floor clear. This machine has a stabilized output of 100 to 200 r per minute at an energy of 8 MeV at an f.s.d. of 1 metre, a performance which is entirely satisfactory.

The extension of the principles used in the M.R.C. linear accelerator led to the design of a very compact and mobile 4 MeV machine. Much useful information has been gained during the construction of the M.R.C. machine which has helped in the final design of the 4 MeV linear accelerator. This design was accepted by the Ministry of Health, and five such machines are being constructed, the first of which is now nearly ready for test.

The development of the high flux heavy water pile at Chalk River, Canada, has made possible the production of radioactive cobalt sources of such intensity and compactness that they can be used for telecurie units working at a focus skin distance of 70 cm. The dose distribution from such apparatus is comparable with that of a 2 MeV X-ray machine. This opens up new possibilities for the provision of a penetrating radiation from a relatively simple apparatus. The complexity here, however, lies in the pile itself which is used for the activation of the cobalt. It is at present somewhat uncertain how many such sources can be activated with the necessary high activity from one pile.

There is little doubt that we are only at the beginning of a supervoltage era. Large and expensive though supervoltage equipment is, the high cost is to a great extent offset by the much greater number of patients it is possible to treat on such a machine, as compared with the routine 200 kV apparatus.

It is hoped that with facilities for treatment by many millions of volts, we shall be able to deliver and control the dose to the tumour with the same precision and ease previously only possible for superficial tumours. One advantage which is certain is that the patient can be treated with a much greater degree of comfort. The reduction in skin reaction itself is a major contribution to the value of X-ray therapy and it can be safely assumed that the lower energy absorption in bone will also lessen the risk of bone necrosis and so contribute to the success of treatment.

The aim of all the technical advances I have just described has been to ensure that the whole tumour shall receive an adequate dose of radiation with a minimum amount of damage to surrounding normal tissues. With the advent of radioactive isotopes came the hope that this same end might be attained by chemical means in that some radioactive element or compound might be selectively concentrated in tumour tissue.

If the tumour dose is of the order of 6,000 r and the permissible dose to the whole of the body no more than 300 r, then for therapy to take place by an isotope the concentration in the tumour must be at least twenty times greater than that of the average concentration in the rest of the body.

So far as malignant disease is concerned, the only therapeutic application of radioactive isotopes which has met with any real degree of success has been the treatment of some cases of carcinoma of the thyroid. The selective concentration here takes place simply by reason of the specialized biochemical reaction which occurs in the thyroid gland involving the element iodine. Unfortunately, however, the majority of thyroid tumours are so anaplastic and undifferentiated that they have lost this specialized function and there is, in such cases, no appreciable uptake of iodine at all. Even in the differentiated tumours where iodine uptake is still retained, an important point to remember is that the treatment of cancer of the thyroid depends on the total destruction of all functional thyroid tissue, whether it be in the gland itself or in functional metastases. Since it is possible for the patient to live normally without any thyroid tissue, provided he is maintained on the appropriate hormones, this total destruction of all thyroid tissue does not matter. There are few other tissues in the body, however, whose total destruction could be tolerated. This fact considerably reduces the possible exploitation of the affinity of particular tissues for particular elements or compounds.

Apart from this, the much greater problem has to be faced of administering a radioactive material in such a form that there is not only an affinity for the particular tissue in question but also the required differential uptake between normal and malignant tissue. This involves a much greater knowledge of the metabolism of both normal and malignant tissues of various kinds than exists at present, and the most important use of radioactive isotopes is almost certainly their employment as a research tool for the biochemical studies which must be carried out before this knowledge can become available.

It is possible, to a certain extent, to overcome the difficulty of whole body radiation or the total destruction of the treated tissue by exploiting the difference in the fate of administered isotopes, dependent on their physical, as distinct from their chemical, form. An example of this is the use of isotopes in colloidal form. For instance, large particles, or gels, are trapped in the pulmonary capillaries and tend to collect in the lungs. The treatment of carcinomatosis by instillation of colloidal gold into the peritoneal cavity is well known. It is exceedingly difficult to employ these treatments on any other than a very empirical basis because of the impossibility of obtaining any reliable physical data concerning the radiation dosage received by tissue treated in this way.

Finally, there are a number of techniques where radioactive isotopes are employed as substitutes for radium and radon. Examples of this are the use of cobalt wire instead of radium needles and the use of solutions or gases in balloons in intracavitary radiation and, of course, the use I have already mentioned, of radioactive cobalt instead of radium in telecurie units. There is nothing fundamentally new in these methods but they offer important practical advantages.

The use of isotopes for the treatment of certain non-malignant conditions is much more promising at present, because the aim here is to affect function rather than to achieve total destruction, so that the requirements with regard to selective concentration are not nearly so stringent as is the case in malignant disease. Moreover, in such examples as thyrotoxicosis and polycythæmia, the target tissue, in this case the thyroid and the bone-marrow, as a direct consequence of the disease which is being treated, has a greatly increased affinity for the isotope. It is probable that a greater knowledge of the physiology and response to radiation of the various types of tissue gained by using isotopes as tracers will lead to the discovery of other therapeutic applications of this type.

The following are a few interesting examples of the applications which have been made of isotopes to general medical problems. Radioactive sodium has been used to develop a method of comparing the placental blood flow in normal and hypertensive patients. It has been demonstrated that the placental ischæmia which was thought to occur in pre-eclamptic patients did, in fact, exist, in that the placental blood flow was only about one-third of that in normal women. In addition, it has been shown that the same degree of placental ischæmia occurs in patients with chronic hypertension, indicating that the hypertension is probably a cause rather than a result of the reduced placental blood flow. Arising out of this work, it became necessary to devise a simple technique for the localization of the placental site and a method, using radioactive sodium, is being developed which makes possible the diagnosis of placenta prævia with an accuracy equal to that obtainable by X-ray diagnostic methods.

The local tissue clearance of radioactive sodium has been applied to tubed skin pedicles, initially to meet the need of a reliable diagnostic test which would enable the plastic surgeons to assess the circulation in a skin graft before its transfer. The availability of a quantitative test, however, has made possible the scientific study of many of the practical problems arising in skin-grafting operations. It is now possible to carry out such procedures with fewer operations and with a substantially reduced period of stay in hospital for the patient.

By the use of radioactive phosphorus a simple yet accurate method has been developed for measuring the circulating red cell volume. The availability of this method has enabled much information to be obtained on red cell and plasma volume in newborn infants for which no reliable data had previously existed. It has also enabled red cell volume measurements to be carried out for evaluating the result of isotope therapy in polycythæmia; these blood volumes have been found to differ materially from those anticipated by indirect methods.

The tracer applications of radioactive iodine in the assessment of thyroid function are well known.

These are just a few examples of the use which has been made of radioactive isotopes in tracer investigations. Many tentative proposals await investigation when short-lived isotopes become available from the M.R.C. cyclotron.

I have attempted to trace the development of the great advances which have been made in radiotherapeutic technique over the past one or two decades. I would like now to consider just what has been achieved by these advances in technique. The first question that one naturally wants to answer is whether these great advances in technique have resulted in any correspondingly great improvement in the cure rate of cancer. When in 1945 we made a comparison of the clinical results obtained in the Unit in more recent years in the treatment of cancer of the mouth and throat with those obtained more than ten years previously, it became clear that the great advances which had been made in the technique of treatment in the intervening years had not resulted in any correspondingly large increase in the proportion of patients cured. It appeared that further improvement in the distribution and control of dosage were not the only matters, nor even the most important, which should be considered in future research in radiotherapy.

It was thought possible at one time that supervoltage X-radiation might have a different biological effect from that of 200 kV X-rays. If this were so then supervoltage therapy would mean something more than a purely technical advance. In order to get an answer to this question we carried out in the Unit a clinical experiment to compare the results obtained by using 200 kV and the gamma rays of radium which are equivalent approximately to X-rays produced at about 2 MeV. In the experiment two series of patients were treated, one with an X-ray beam and one with a gamma ray beam, and every effort was made to eliminate variables in the two series of patients treated. The results of this investigation did not show that the wavelength of radiation *per se* within the limits of the experiment, i.e. 200 kV and approximately 2 MeV, had any significant effect on the clinical results. We therefore concluded from our experiment that the great advantage to be expected from the use of supervoltage therapy was not in any different biological effect, but in the enormously improved dosage distribution which could be obtained by this means. The advance is a purely technical one resulting in a better dose distribution. Although we can be sure, as I have already mentioned, that it will be possible to treat patients with a much greater degree of comfort, we have, I think, no reason to believe that there will be any spectacular improvement in cure rate by the use of the technical advances inherent in supervoltage therapy.

The comparison of cure rates obtained at different centres is extremely difficult due to a lack of uniformity in the presentation of results. There is also a lack of published figures for many sites treated because so many centres only publish the results of special series of cases and not the results of all their work. This fact is internationally recognized as an outstanding problem and it is to be hoped that, in the near future, great improvement will occur in the presentation and analysis of results of the treatment of cancer.

So much valuable information could be gained from the clinical work which is in progress in so many centres, if work could be based to a much greater extent than it is at present on making definite comparisons between different methods of treatment and getting a decisive answer. Clinical experiments are often more difficult than laboratory experiments. The classical method of clinical research was that of observing the individual patient's reaction to treatment and drawing conclusions from the reactions found to be common in relatively small groups of patients. The modern method tends to be the simultaneous comparison of alternative treatments applied to properly randomized groups of patients. The simultaneous trial of two alternative treatments is a much more satisfactory procedure than the comparison of a new treatment with results obtained in an earlier period or in another institution. Much progress could be made in clinical radiotherapy if there were planned experiments of this type. We ought to look forward to even greater co-operation with our surgical colleagues and be prepared to make comparisons between the results of surgery and radiotherapy by means of planned experiments: for example, in the simplest case, by arranging for patients who have been assessed as operable, to be allocated objectively either to surgery or radiotherapy as the primary means of attack. We should, by this means, finally get a decisive answer to many questions which have been debated over a long period of years.

In Fig. 1 the results of treatment of some 1,748 cases of carcinoma of the laryngo-pharynx are shown. These cases were treated at different centres in this and other countries by many different methods. The outstanding fact revealed by a study of these figures is that in no centre are results obtained in which there is a significant difference from any other centre or from the overall result. It seems reasonable to conclude that some factor in the tumour itself, a factor of which unhappily we are at present ignorant, has a far greater influence on the final prognosis than the particular form or technique of treatment employed.

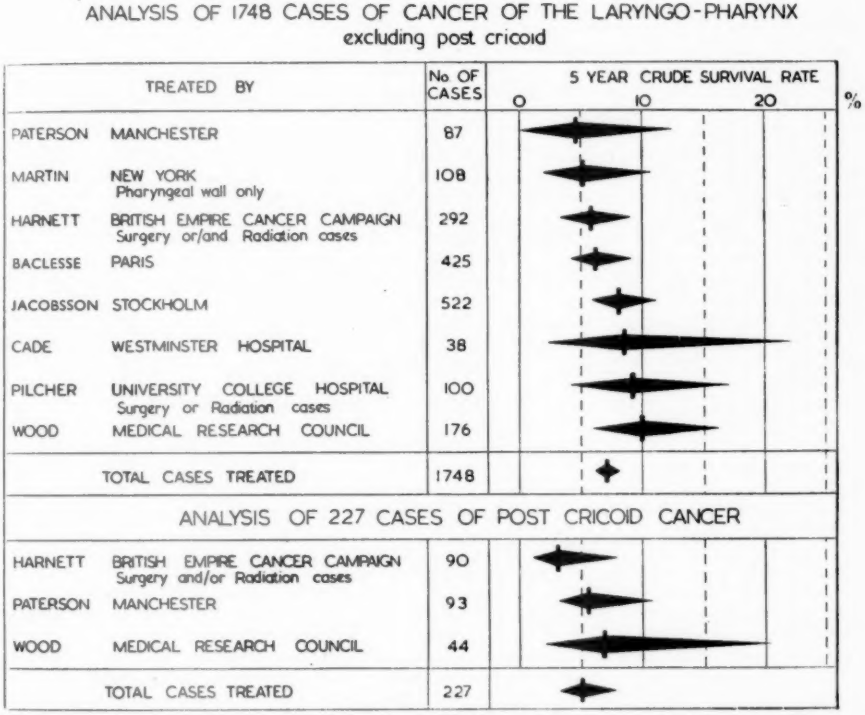
ANALYSIS OF 1748 CASES OF CANCER OF THE LARYNGO-PHARYNX
excluding post cricoid
TREATED BY
No OF CASES
5 YEAR CRUDE SURVIVAL RATE
0
10
20
%
PATERSON MANCHESTER 87
MARTIN NEW YORK Pharyngeal wall only 108
HARNETT BRITISH EMPIRE CANCER CAMPAIGN Surgery or/and Radiation cases 292
BACLESSE PARIS 425
JACOBSSON STOCKHOLM 522
CADE WESTMINSTER HOSPITAL 38
PILCHER UNIVERSITY COLLEGE HOSPITAL Surgery or Radiation cases 100
WOOD MEDICAL RESEARCH COUNCIL 176
TOTAL CASES TREATED 1748
ANALYSIS OF 227 CASES OF POST CRICOID CANCER
HARNETT BRITISH EMPIRE CANCER CAMPAIGN Surgery and/or Radiation cases 90
PATERSON MANCHESTER 93
WOOD MEDICAL RESEARCH COUNCIL 44
TOTAL CASES TREATED 227

FIG. 1.—The percentage five-year survival rates[1] of different groups of cancer of the laryngo-pharynx and post-cricoid cancer are shown with the confidence limits for each group. The percentage survival rate is indicated by the small thick black vertical line and the confidence limits for each group are represented by the horizontal lozenge. These confidence limits are seen to vary in length according to the number of patients in each group—the larger the number of cases the nearer do the confidence limits approach the estimated survival rates.

We may well doubt whether all the efforts which have gone into making great technical improvements in radiotherapy have yielded a commensurate return.

While the percentage cure rates show little change it is well to remember that accurate dosimetry and beam direction make it possible for treatment to be given to large numbers of patients in accordance with techniques based on the observation and experience of the most reliable radiotherapists.

Thus, even if we do no more than hold the percentage cure rate constant, the number of individuals cured of their disease will rise year by year in proportion to the number treated, so that in terms of human lives something worth while may be said to have been accomplished.

[1] *Note.*—When a limited number of patients has been treated, the five-year survival rate for such a group does not enable us to say with certainty what the survival rate would be if a much larger group of patients were treated—that is to say, what is the true survival rate for the method of treatment. Knowing the number of patients treated and their five-year survival rate, however, from elementary statistical theory one can quote limits between which the true value will lie in most cases. We wish to keep the limits as close as possible in order to detect small differences between methods of treatment and we must therefore adopt by convention some "measure of confidence". If we accept limits within which the true value should lie in 19 cases out of 20, we shall be following ordinary statistical practice. Such confidence limits are indicated by the length of the black lozenge in the diagram.

The treatment has been made measurable and repeatable. This accurate dosimetry and beam direction have been indispensable in enabling us to make comparisons; for instance it has been shown, at least as regards the oral cavity, that when treated with the same dosage, the radiocurability of primary tumour and metastases is similar. Again comparing the response of two tumours to the same treatment we have been able to show that two tumours of apparently identical histology and similar clinical appearance may respond quite differently to the same treatment. It is only as a result of making the physical aspects of radiotherapy quantitative that it is possible to assert that we are really up against a biological problem and can make some statement about the elements of this problem.

Further progress in radiotherapy is most likely to come from a better understanding of the mode of action of radiation on the body.

A study of the general metabolic effects produced in patients by radiation presents considerable difficulties. When we study the effect of radiation on one system within the body, for example the extracellular fluid, the problems of interpretation become very complex indeed. It is virtually impossible to separate out what may correctly be regarded as radiation damage from the response of the whole body to that damage. Nevertheless, a study of the whole body response of patients has recently yielded most interesting results. It has been shown that a response as complex as radiation sickness can be studied in a quantitative manner and when this is done interesting correlations are revealed between the response, the dose and the size of the patient. These point to likely sites of origin of the initial disturbance and so carry the investigation to further levels.

Considerable progress has been made in the study of cell metabolism and research in this field has yielded much valuable information. Tracer doses of radioactive isotopes have been combined with microscopical observations to study the dynamics of metabolism of irradiated tissue by the autoradiograph technique. As yet the gap between this type of research and clinical practice has not been bridged. It is, I think, fair to say that so far it has not proved possible to make any clinical application of the knowledge gained with a consequent improvement in cure rate. Several milestones, however, have been passed. It has been recognized that the biological response to a given dose may be correlated, except in very rare instances, with the spacing of the ions along the tracks of the ionizing particles. This has re-emphasized the fact that there is no great difference in biological efficiency between 200 kV X-rays and those generated at much higher voltages. It has, however, indicated that the biological efficiency of neutrons relative to X-rays is greater by a factor of between 5 and 10. Whether the radiobiological difference between neutrons and X-rays can be made advantageous to the therapist or the reverse, is for a clinical trial to determine. The one clinical trial which has already been carried out in the U.S.A. clearly suffered from a lack of good neutron dosimetry at that time.

Our physical ideas about the distribution of ions along particle tracks have advanced hand in hand with an experimental study of the chemical effects of different types of radiation. Very valuable work has been done in radiation chemistry and physical reasons for the very marked difference between the characteristics of chemical changes produced by high voltage X-rays on the one hand and neutron and alpha particles on the other hand, are now apparent. Ever increasing knowledge is accruing which emphasizes the importance of radiation chemistry as a link between the original ionization and the eventual biological response not only in a part of the organism but in the organism as a whole.

It has been known for some time that the effectiveness of a dose of radiation is modified by the amount of dissolved oxygen present. Recently, this effect has been studied both in plant tissues and mammalian tissues and the same effect has been shown in all the tissues so far investigated. If dissolved oxygen is present in the tissue at the time of radiation, the biological efficiency of the radiation is about two and a half times greater than when oxygen is not present. It may be concluded, therefore, that dissolved oxygen plays a part in handing on the energy of radiation to the living cell. The importance of this knowledge lies in the fact that it may lead to our being able to understand, and possibly control, for the first time an intermediate step in the action of X-rays. It may even be possible to utilize this knowledge in clinical practice, the prospect of success depending on the existence of a differential effect between normal and malignant tissue. As our knowledge extends, a further variable may be given to the radiotherapist, which may enable him to influence the biological efficiency of radiation. It is indeed a dynamic position in which we find ourselves to-day—with a constant interlinking and exchange of ideas between workers studying radiation effects from so many different viewpoints; the chemical effects, the effects on cell metabolism and finally the whole body response to radiation—a state of affairs which is full of possibilities.

The dream of the radiotherapist in former decades of obtaining an X-ray beam which would deliver a high dose to deep-seated tumours without damaging the skin has now been achieved. With this, however, has come the realization that improved technique will not materially increase the cure rate of cancer.

The dream of the radiotherapist to-day is that we may find ways of influencing the biological response of tissues to radiation and that it is in the realization of this hope that future progress in the next decade is most likely to be achieved.

"For each age is a dream that is dying,
Or a dream that is coming to birth."

—*A. W. O'Shaughnessy.*

Section of General Practice

President—E. P. Scott, M.B., M.R.C.S., L.R.C.P.

[*April* 15, 1953]

DISCUSSION: VAGINAL DISCHARGE AS SEEN IN GENERAL PRACTICE

Dr. Marion Ravell: About twenty-five years ago, before the days of the sulphonamide drugs and antibiotics, I examined about thirty to forty women daily over a period of three years, all complaining of vaginal discharge. At the time I had the services of a pathological laboratory round the corner, where smears were expertly examined, and a diagnosis made for me. Each predominant infecting organism appeared to produce its own variety of discharge of similar colour, consistency and odour, so that the pathological report confirmed the diagnosis rather than made it.

Vaginal discharge is a common complaint amongst women of all ages, and may be a symptom of local or general disease, physical or psychological. A great many discharges are readily amenable to simple treatment, and the relief given to the patient is out of all proportion to the seriousness of the complaint. In fact, I have found that this is one of the conditions in which the gratitude of the patient is ample reward for the time and trouble spent in treatment.

I am frequently surprised myself, not only at the improvement of the local condition, but the improvement in the general outlook and feeling of well-being of the patient. It is so marked, and happens so often, that I now think of vaginal discharge as seen in general practice as being a psychosomatic disease in about 50% of the cases seen.

I always insist on examining a patient who complains of a vaginal discharge in my own room at the Surgery, where there are the essentials ready at hand for an adequate inspection. Owing to the really good propaganda during the last war and since, most women go straight to a V.D. Clinic if they have reason to think that they have caught gonorrhœa or fear that they have done so. The speed and efficacy of the modern treatment has altered the attitude of the general public to venereal disease, and they seek treatment more readily.

Gonorrhœa can be dismissed with the one word penicillin, or perhaps with two, for the sulphonamide drugs still have their uses. It is fantastic to think that only about ten years ago, months and sometimes years were spent in frequent douchings, swabbings and paintings with the occasional reward of a satisfactory "test of cure" which took six months to complete after the cessation of active treatment. No wonder they hung back from having their worst fears confirmed, and no wonder treatment in so many cases was never completed and the disease continued to be passed round.

The question of a chronic gonorrhœal infection must always be borne in mind, especially if there is a suspicious history, and smears should be taken. It is in these cases, however, that one so often gets a report showing "pus and mixed organism, and no intracellular diplococci". The complement-fixation test can be of value then in deciding if the discharge is due primarily to a gonococcal infection.

The vagina is a passage about 3 to 4 in. in length, extending from the vulva to the uterus, from open unsterile surroundings to the sterile body of the uterus, tubes and peritoneum. Normally it is only a potential space, but capable of distension as the series of transverse folds or rugæ of the lining mucous membrane are opened up, as in childbirth. This mucous membrane is covered by a thick layer of stratified squamous epithelium, supported by loose, white fibrous tissue, and plain muscle fibres. This also supports the plexiform arrangement of the vaginal veins which drain into branches of the internal iliac veins. Anteriorly, the bladder and urethra and posteriorly, the rectum, are intimately connected with it. There are no glands in the mucous membrane, and the normal protective vaginal secretion is derived partly from the mucous discharge from the cervix, and a transudation from the vaginal epithelium. This secretion is white and coagulated in appearance and acid in reaction. This acidity has an inhibiting effect on the growth of pathogenic organisms, though the vaginal bacilli of Döderlein thrive in this medium. Smears of the normal secretion show squamous-cell debris and the large Gram-positive Döderlein bacilli, and evidence of these show that the secretion is healthy and normal. They are destroyed by secondary infecting organisms very easily.

The constant washing away of the acid transudate, and the Döderlein bacilli by the frequent and indiscriminate douching of ladies who like to feel clean, is a common cause of vaginal discharge. The more they douche, the more they complain of discharge! Usually this type of patient is fastidious, and the more disturbed and anxious they become about this minor discomfort, the worse

it becomes, until they become obsessed by it and are convinced that they have a cancer, or are unclean and, therefore, outcasts. The anxiety state which develops is out of all proportion and far removed from the simple cause, which may take a long time to elucidate.

On the whole, I find that I have cured more vaginal discharges by stopping patients douching than by ordering them to do so. It is a dirty habit. This type of patient too often feels that the stronger the douche the better it must be for them. If constantly used, and too strong, it will expose an irritated mucosa to the onslaught of the staphylococci and streptococci and *Bacillus coli* that are always lurking about in those parts, whilst the poor Döderlein bacilli are washed away in the floods. The same applies to the constant use of tampons, pellets and pessaries. Overtreatment is the danger, and I find it better to avoid giving patients of this type a supply of anything to carry on themselves with the treatment, as they will always do too much and perpetuate the discharge.

The vagina being so closely related to the lower urinary tract and to the rectum, its protective transudate must be affected by the condition of these organs, by infection or congestion of them. The woman who spends the day with a heavily loaded rectum and never evacuates completely must expect an increase of vaginal secretion. A bacilluria nearly always produces an increase, and *B. coli* can be demonstrated on a stained smear.

The vagina, in addition to these hazards, is also part of the sexual organs and is, therefore, influenced by the emotional state. It weeps with frustration, overstimulation, despair or depression. The Bartholin glands on guard at the vaginal orifice add their mucoid discharge at all times of sexual excitement. This mucus is a useful and necessary lubricant during intercourse, but can be a very uncomfortable and disturbing phenomenon to the young woman during a long engagement. I am often consulted by young patients because of this type of discharge, and it can be the cause of much unhappiness and anxiety.

In addition to the emotional causes of increased vaginal secretion, there are the local irritants. A cause that is comparatively new is nylon. The wearing of nylon panties can produce in some women a vulvo-vaginitis with a good deal of discharge. I suppose that this is an allergic reaction.

Foreign bodies left in the vagina and often forgotten will soon cause an offensive discharge. I have removed contraceptive caps and condoms which have been forgotten, as well as Tampax and tampons, with a dramatic cure of the "terrible disease". I remember seeing a woman who had suffered great discomfort for three years, and such agony of mind that she had prepared her family for her approaching death from cancer so convincingly, that they quite overlooked calling in a doctor. Finally I removed a stinking ring pessary with difficulty, which had been inserted over three years previously at a hospital, and the patient had quite forgotten the fact and any instructions that she had had at the time. The cure was quite spectacular!

Repeated local trauma, such as abortive and unsuccessful attempts at intercourse, will produce a discharge, partly an increase of the normal, because of the frustration and emotional disturbance which is usually present in a greater or less degree during these episodes, and also a superimposed secondary infection may develop, because the bruised and damaged hymen offers a suitable culture medium for staphylococci, *Bacillus coli* and also the *Trichomonas vaginalis*. This type of discharge may also follow two or three weeks after marriage, and gonorrhœa must be excluded before tragedy supervenes and a marriage spoilt needlessly. Masturbation may, in the same way, produce this type of discharge, and the treatment must deal chiefly with the psychological state of the patient.

The excessive loss of normal secretion in adolescence, the young girl's leucorrhœa, is a problem on its own. Careful inspection is necessary, though not the passing of a speculum, and the less treatment given locally, the better. The complaint about the discharge varies both with the fastidiousness of the patient and her attitude to approaching maturity. A resentful and fearful attitude towards her periods will make her much more aware and distressed by what may be a normal secretion. A girl of 15 who insisted that the discharge was so bad that she had to wear a pad all the time, was so resentful of growing up, that she inflicted this discomfort upon herself. After reassurance, she was persuaded to stop wearing a pad, to bath daily, and rapidly her symptom vanished. The change-over from active school life to a sedentary occupation, with little exercise, and the constipation that so often follows from this change to a less active life, will produce the triad of the loaded colon and rectum, back-pressure and congestion in the pelvis, excessive discharge from the cervix and transudate from the vagina. The treatment is simply one of hygiene and adequate exercise.

The high carbohydrate and low protein diet that we have all had to indulge in owing to rationing, particularly affects the young. Restriction of starchy foods will help in the treatment of a persistent nasal catarrh, and it has certainly been found helpful in vaginal catarrh. All the mucous membranes appear to work overtime when there is an unbalanced diet with too much starch. Where there is impaired sugar tolerance, and diabetes, there is the frequent complaint of vaginal discharge which may not be accompanied with the pruritus associated with diabetes.

Anæmia is also a factor to be dealt with in these cases. The pale, sluggish, tired girl, too tired to play games, too tired to evacuate properly, will nearly always have an excess of secretion.

If regular exercise is difficult to take in the form of games, walking and other sport, I have found that the pamphlet used in schools for the alleviation of dysmenorrhœa, setting out a series of simple exercises that can be done daily in the bedroom to stimulate the pelvic circulation, is very useful to

give to those girls with leucorrhœa. This menstruation leaflet for schoolgirls and a slightly different one for working adolescents are both published by the Medical Women's Federation.

In addition to these non-specific causes of discharge, there may be an infection of the vagina itself, the most usual being the *Trichomonas vaginalis* and the *Monilia albicans*. Lesions in the walls, such as epithelioma and malignant ulceration, &c., can be seen on inspection to be surgical conditions and are outside the scope of this paper. They should be referred to the gynæcologist at once.

The vagina may act as a viaduct and merely convey discharge from the cervix and uterus and tubes. Cervicitis and erosions are usually seen in multiparous women and are the result of infection and laceration of the cervix following childbirth. Carcinoma of the cervix produces a thin offensive blood-stained discharge, and again is a case for immediate reference to the gynæcologist.

If there are no obvious lesions in the vagina or cervix, then the uterus and its appendages are guilty. Conditions such as pyometria, infected retained products of conception, endometritis, submucous polyp and again carcinoma must be considered. Lastly tubal infections, such as tubercular, gonococcal, streptococcal infections, and again carcinoma can all produce discharges which present at the external os and give rise to a vaginal discharge. Unless carefully looked at, and its site of origin discovered as far as possible by inspection through a speculum, it may be overlooked as a symptom of serious disease, where delay in treatment may be catastrophic to the patient.

The two important and most frequent organisms causing discharge are the *Trichomonas vaginalis* and the *Monilia albicans*. Both parasites produce highly irritating profuse discharge with an associated vulvitis. Both need some interference with the squamous health of the vagina and alteration of the pH of the secretion to thrive and become troublesome, as both can be demonstrated in apparently healthy vaginæ with no excessive discharge. Both produce a discharge which is absolutely characteristic in appearance, and though in hospital practice the presence of the parasite is quite properly confirmed by fresh hanging-drop preparation and smears, I have found that the discharge once seen is diagnostic, and treatment can be started at once.

The appearance of the discharge in a trichomonal infection is a bright, yellow, thin frothy fluid. The amount of frothiness varies, but is always present. The vulva is red, swollen and sore, the vaginal walls are reddened and dull, with scattered, deeper, red spots over the fornices and upper vagina. Gentle swabbing away of the discharge with warm saline swabs or lactic acid swabs, and the insertion into the fornices of two or three S.V.C. pellets at the time of the examination will produce relief. The patient can insert these pellets daily for a week, when a further inspection will usually show great improvement. A treatment just before and immediately after a menstrual period gives the best results. If the discharge is very profuse a few douches of two pints of a lactic acid solution should be advised, but the douching is only for the quick removal of the highly irritating discharge and is not of real value in treating the condition.

The discharge due to a thrush infection is thick, white and curdy. The vulva is swollen and sore, and the irritation may be intense. This irritation is usually the symptom most complained of, as the discharge is so thick and tenacious it is not until the labia are separated that the cheese-like substance, clinging around the introitus, is seen. The whole of the vagina may be packed with it. No douching in the world will remove it, but by swabbing first with hydrogen peroxide, then with a bicarbonate of soda solution, most of the flakes will come away, leaving the vaginal walls reddened and spotty. The walls can then be painted with an aqueous solution of 1% gentian violet. There is nothing local for the patient to do, and two or three treatments will produce an amazing improvement. This type of discharge is commonest in pregnancy, and an untreated discharge of this type can make the life of a pregnant woman almost unbearable.

A glycosuria is often found associated with a yeast infection and should be investigated.

The cervical erosion is always with us. It is an area around the external os denuded of its squamous epithelial covering, exposing the underlying tissues of the cervix. It is usually the result of infection, but it may also be due to impaired vitality of the cells, due in turn, to impaired vitality of the patient. This later type I have found to clear up without local treatment in a surprising way if the general condition of the patient is adequately dealt with. A bright red area around the os, soft and velvety to the touch, and with some mucopurulent discharge due to secondary infection, is often found after long, debilitating illness, and is the direct result of it. Inspection of the cervix later, after general recovery is complete, will show that the erosion has healed also.

The most usual type is found as a result of post-partum injury or infection, and is associated with low backache, and vague pelvic discomfort, as well as a mucopurulent or purulent discharge, and certainly requires treatment. It is always worth while trying the simple things first before referring the patient to the gynæcologist for cauterization, amputation of the cervix, &c. I find that the application of pure Negatol after swabbing the cervix clean on three or four occasions produces improvement in a great many cases. I also give glycerine pessaries, large two-drachm size, to be inserted well up into the vagina nightly, but I avoid telling the patient to douche, and stop her if she is already doing so. There are, on the market now, tubes and applicators containing triple sulpha cream. These are good, but I do not find that the results are any better than Negatol or glycerine pessaries, and the latter treatment is much cheaper.

A cervical polyp can cause a very distressing blood-stained discharge, and twisting off the polyp with sponge holders, and touching the bleeding base with Negatol is usually sufficient to produce a "cure". If it is particularly fleshy or firm I send it to be sectioned, and always warn the patient that if it should recur, further investigation must be made.

A senile vaginitis again may cause a great deal of real anxiety, in addition to the discomfort, as it is often blood-stained, and arises at a time when women feel that they are particularly prone to the cancer. After the menopause the protective acid secretion and transudate change due to the atrophy of the vagina and uterine appendages, the nutrition is interfered with, and secondary organisms can readily multiply and give rise to an irritating discharge. Œstrin pessaries, and œstrin by mouth or by injection for a short period restores the vitality of the vaginal mucous membrane, and enables it to overcome the invading organisms. A chronic urinary infection and diabetes must, of course, be excluded.

Mr. Alan Brews: Vaginal discharge is a common symptom and cases found to be resistant to simple treatment are frequently referred to Gynæcological Out-patient Departments.

Dr. Ravell contends that, by careful yet simple clinical examination of the genital tract, it is usually possible to arrive at a diagnosis of its cause with sufficient accuracy for ordinary clinical purposes. This is largely true as regards discharges due to recent acute infections where the clinical characters have not been modified by treatment. At the other end of the scale, however, there are many cases in which it is difficult to arrive at a satisfactory diagnosis even after extensive laboratory investigations.

General practitioners do, in fact, refer many patients to hospital without making any clinical examination of the genital tract, preferring to spare them the discomfort, inconvenience and embarrassment of a double examination. Treatment is not infrequently prescribed without diagnosis by clinical examination—certainly a reprehensible practice.

Simple leucorrhœa (by which I mean an excess of the normal secretion of the genital tract) can be diagnosed by its naked-eye appearance and does not merit bacteriological investigation in a hospital out-patient department. Its causes are manifold but it is physiological if related to sexual emotion or pregnancy and morbid when evoked by an anxiety state, a too sedentary life, hormone imbalance or by local irritants in the vagina. Dr. Ravell's approach to some of these leucorrhœas as minor psychosomatic disorders is sound as they are more likely to be alleviated by a little common-sense advice than by elaborate investigation and treatment applied to the genital tract.

The patient's own diagnosis of vaginal discharge should not be accepted without confirmation as in many instances no abnormal discharge can be found on clinical examination or, alternatively, a patient will deny its existence when large quantities of purulent exudate are present.

Very often the question will arise of underlying venereal disease. It is then of great practical value if a full investigation can be carried out in the Gynæcological Clinic or in a small "reference" clinic with a venereologist in attendance. Such a clinic should not be situated in the Department for Venereal Diseases and the patient should only be referred there after the diagnosis has been confirmed. In this way a diagnosis of venereal disease can be excluded without the necessity of raising its possibility with the patient.

Infection with *Trichomonas vaginalis* may be associated with gonococcal infection, and diagnosis of the latter condition may, therefore, prove difficult. The reasonable exclusion of venereal infection requires at least three sets of films and cultures from the genital tract at intervals and at least one blood examination for Wassermann reaction and gonococcal-fixation test.

In a recent survey of a group of patients complaining of vaginal discharge I. Donald found infestation by *Trichomonas vaginalis* in 37·4%. The acute vaginitis that may result from such infestation may cause a copious purulent discharge and the vagina may be so acutely tender that satisfactory examination can only be carried out under anæsthesia. The origin of the infection is often obscure but local trauma from intercourse or attempted intercourse may be a factor and, to this extent, it is in fact a venereal disease. The alteration of the pH of the vaginal secretion from the normal 4–5 to the lower acidity of 5·5–6, which occurs in association with menstruation, facilitates the development of the organism.

Mr. McKim McCullagh has found evidence of infestation by *Trichomonas vaginalis* in 13% of the hospital patients and 11% of his private patients and he regards the ring type of pedestal seat provided in most public lavatories as a common means of spreading this infection.

Monilial (yeast) infection of the vagina tends to occur during pregnancy and when glycosuria is present. The development of this infection is favoured by high acidity and most cases will respond to local cleansing with a weak solution of sodium bicarbonate and subsequent painting with a 2% aqueous solution of gentian violet. Elimination of the spores is difficult, and continued and thorough local treatment to the cervical canal as well as the vagina is necessary to achieve this.

Purulent infection with pyogenic bacteria such as *Staphylococcus aureus*, *B. coli* or *B. proteus* are all less common causes of vaginal discharge and are best treated with local and systemic chemotherapeutic agents to which the particular cultured strain is found to be sensitive. It must be remembered that a watery or purulent vaginal discharge is at times the first and sometimes for many weeks the only symptom of malignant disease of the genital tract.

Section of Anæsthetics

President—M. D. Nosworthy, M.A., M.D.

[*May* 1, 1953]

Some Electroencephalographic Changes Associated with Induced Vascular Hypotension

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Extremes of vascular hypotension lead to ischæmic anoxia, and so in using a technique of induced vascular hypotension, in which the blood pressure is deliberately reduced to low levels, limits of safety must be determined for the various parenchymatous organs of the body. Of all the tissues in the body the brain has the least tolerance of anoxia. In studying the effects of induced hypotension, therefore, it is supremely important to determine the lowest levels of blood pressure at which normal cerebral metabolism can be maintained, both in health, and in the presence of arterial disease. An attempt has been made to do this in three conscious subjects.

Tests for normal cerebral function may be psychological, such as the arithmetical and association tests, or psycho-physical such as the flicker-fusion test (Nilsson, 1953), or purely physical, as in the electroencephalogram or EEG. The last of these seemed preferable for the present investigation, by virtue of its objectivity, and its ability to record fleeting changes of cortical activity.

There is plenty of evidence that the electrical activity of the brain, manifested by the electroencephalogram, can be used as an index of cerebral cellular activity, and that anoxic interference with cerebral metabolism is reflected by changes of electrical rhythm. The effects of ischæmic anoxia have been studied in animals by Beecher, McDonagh and Forbes in 1938. Working with cats they found that reduction of blood pressure below 30 mm.Hg systolic, by bleeding or cardiac tamponade, abolished cortical rhythm, while restoration of the blood pressure was followed by resumption of cortical activity. Sugar and Gerard, also in 1938, obtained similar results by vascular occlusion. Gurdjian, Webster and Stone (1949), investigating the effects of anoxæmic anoxia, found that the inhalation of atmospheres containing 11·6% oxygen caused slowing of the dominant cortical frequencies in dogs, and the time required for recovery of normal rhythm varied with the degree and duration of the oxygen lack.

In man, Davis *et al.* (1938) found that respiration of an 8% oxygen atmosphere for ten to fifteen minutes caused the normal alpha rhythm of about 10 cycles per second to be replaced by slow delta waves of less than 4 cycles per second. Gibbs *et al.* (1940) showed that when the oxygen saturation of the cerebral venous blood fell from the normal level of 65% to 28% consciousness was lost, and the normal alpha rhythm was replaced by delta waves, with reduction of the total electrical energy of the cortex. In the investigation of flying hazards by centrifugal cerebral anæmia (Franks *et al.*, 1945), it was found that loss of consciousness was accompanied by a slowing of cortical frequencies, and that with return of consciousness normal cortical rhythm returned also.

Kaufman and Hoagland (1946) sum up the relationship between the EEG pattern and cerebral metabolism thus: "the frequency of the alpha rhythm is directly proportional to the velocity of a chemical pacemaker or bottle-neck in the serial chain of enzyme-catalysed events involved in cerebral respiration." The dominant frequency is slowed by factors which reduce the rate of cerebral respiration, and accelerated by factors which increase the liberation of metabolic energy in the brain.

From the above results, and those of others such as Noell and Kornmüller (1944), Swank and Foley (1948), Lyman *et al.* (1941) and Iwana (1950), it appeared reasonable to use the electroencephalogram as an index of cerebral cellular anoxia during induced vascular hypotension.

Experimental Methods

A combination of posture, and autonomic blockade by a drug of the methonium group was used to lower the blood pressure of three conscious subjects breathing room air (Enderby, 1950). Electroencephalographic recordings were made continuously before, during, and after the period of induced hypotension.

Pentamethonium iodide (C5) was given intravenously in doses between 40 and 240 mg. in the horizontal position. After the blood pressure had fallen in response to the drug (usually to the level

of 80–100 mg.Hg systolic), the subject was tilted into a foot-down position varying between 5 degrees and 45 degrees, depending on the response obtained.

Results

Case I.—In one normotensive subject it was impossible to lower the B.P. below 80/60, despite a total dose of 240 mg. of pentamethonium iodide given over a period of twenty minutes, and a foot-down tilt of 45 degrees. There was no alteration of the alpha rhythm in this case (Fig. 1).

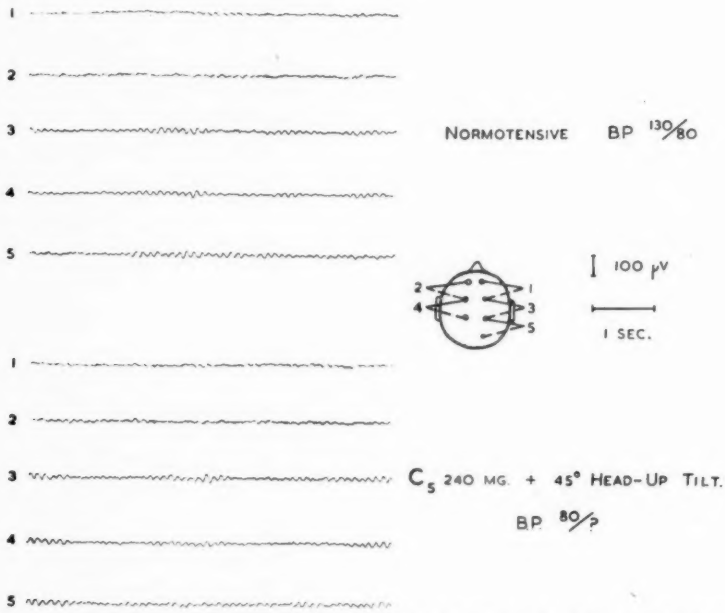

FIG. 1 (*Case I*).—Unchanged EEG in a normal subject before and during moderate hypotension induced by C5.

The other 2 cases are described in detail, and their EEG recordings shown in Figs. 2 and 3.

Case II.—Normal male aged 38, with a resting B.P. of 130/80, and a resting alpha rhythm of 9 cycles per second and amplitude of 40 microvolts (Fig. 2A). 100 mg. of C5 were injected intravenously in divided doses over a period of six minutes, with the subject in the horizontal position. At the end of this time the blood pressure was 90/60, and the EEG pattern was unchanged. The subject was then rapidly tilted into a 45 degrees foot-down position. This was quickly followed by a precipitate fall of blood pressure to unrecordable levels. In the EEG, alpha rhythm was completely abolished, and the record dominated by medium voltage delta waves of 1–2 c/s (Fig. 2B). The subject became unconscious, and developed clonic convulsions involving the face and arms. The tilt of the table was now rapidly reversed to a 10 degrees head-down slope. One minute later the B.P. was 40/?, and consciousness was returning. The alpha rhythm was also returning at its normal frequency of 9 c/s, but with a reduced amplitude and persistence (Fig. 2C). Four minutes later, with the subject in the horizontal position, consciousness had fully returned. The alpha rhythm was restored to normal frequency and amplitude (Fig. 2D), and the blood pressure was 105/70. Thirty minutes later a gradual foot-down tilt to 15 degrees reduced the blood pressure to 55/30, that is, a fall of 61% of the mean arterial pressure. At this point the subject complained of feeling light-headed, and the EEG showed a 40% decrease in the amplitude of the alpha rhythm, although the normal frequency still persisted.

Case III.—Arteriosclerotic man of 57, with a resting B.P. of 200/120, and a resting EEG record of normal amplitude at 7–8 c/s (Fig. 3A). 40 mg. of C5 were given intravenously in divided doses over a period of six minutes, in the horizontal position. The B.P. fell steadily to 80/60, that is, a reduction of 54% of the mean arterial pressure, without any change in the frequency or amplitude of the cortical rhythm. When the B.P. reached 70 mm.Hg systolic the frequency was still unaltered, but there was a reduction of amplitude, particularly in Lead 3. The subject was now tilted into a 5–10 degrees foot-down position. The B.P. fell rapidly. As the systolic pressure passed the 55 mm.Hg level the resting rhythm became replaced by slower waves of greater amplitude. One minute after tilting, the B.P. was 35 mm.Hg systolic (the diastolic pressure could not be obtained). The subject was unconscious, and tonic-clonic convulsions of the face and arms were commencing. At this point the EEG was dominated by slow delta waves of 0·3 c/s, 0·5 c/s and 1 c/s, in irregular combination (Fig. 3B). A slight head-down tilt was now assumed, and oxygen administered. The B.P. rose

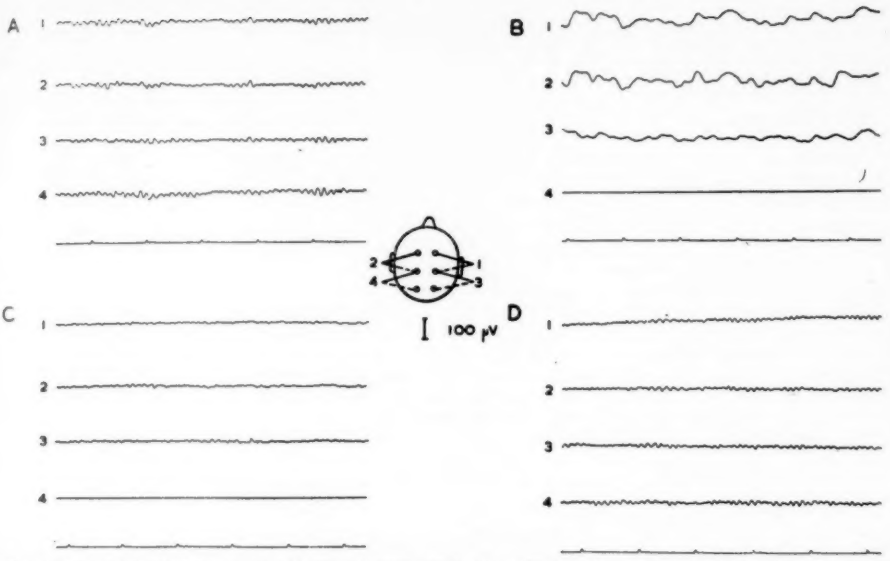

FIG. 2 (*Case II*).—EEG records of normal man, aged 38. Time-marker: 1 second intervals. A, normal resting rhythm of 9 c/s. B.P. 130/80. B, During acute fall of B.P. to unrecordable levels, after 100 mg. C5 and 45 degrees foot-down tilt. Subject unconscious. C, one minute after B, 10 degrees head-down. B.P. 40/?. Consciousness returning. D, Four minutes after C. B.P. 105/70. Conscious. Normal α-rhythm.

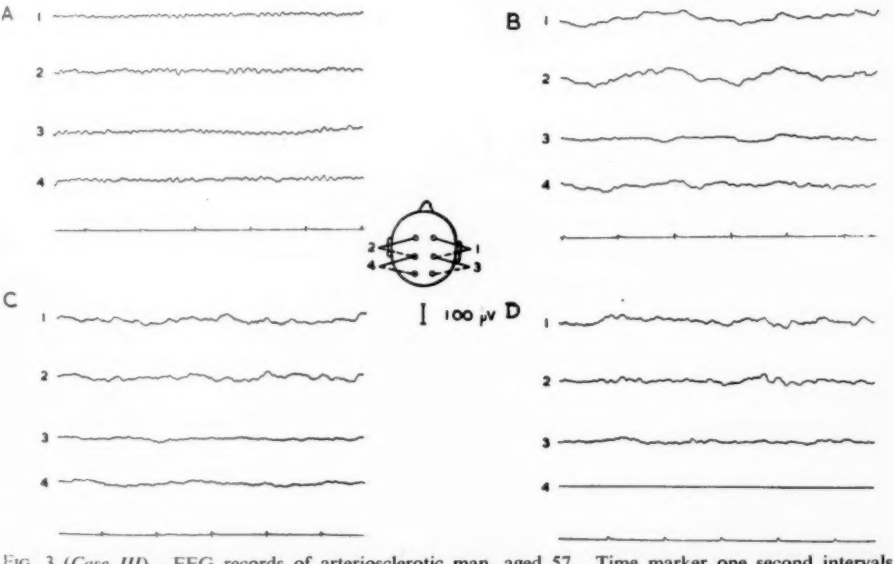

FIG. 3 (*Case III*).—EEG records of arteriosclerotic man, aged 57. Time marker one second intervals. A, Resting record. 7–8 c/s. B.P. 200/120. B, In 5–10 degrees foot-down tilt following 40 mg. C5. B.P. 35/?. Subject unconscious. C, Ten minutes after B, in slight head-down position, breathing oxygen. B.P. 110/75. Consciousness returning. D, Fifteen minutes after C. B.P. 150/85. Conscious.

slowly to 110/75 over the next ten minutes, and consciousness began to return. In Fig. 3C (ten minutes after B) faster frequencies of 2–3 c/s are appearing in the record, which is, however, grossly abnormal. After a recovery period of twenty-five minutes the subject was conscious but euphoric, with a B.P. of 180/85. The EEG was still abnormal, although the very slow activity of 0·3–1 c/s had subsided, and the background frequency was returning to a more normal pattern (Fig. 3D). A follow-up tracing taken seventeen hours later showed complete return to the normal rhythm.

Discussion

Conclusions to be drawn from an investigation of the cerebral circulation and cerebral metabolism in conscious subjects can apply only loosely to the assessment of conditions under general anæsthesia. Schmidt (1950), and Wechsler *et al.* (1951) have shown that under light thiopentone narcosis cerebral metabolism is reduced by almost 40%, so that discrepancies between oxygen supply and demand are less likely to occur under anæsthesia than in the conscious subject. Any conclusions to be drawn from the preceding experiments will be made with this reservation in mind.

The immediate results of acute hypotension were the same in Case II and Case III. Consciousness was lost, followed by the onset of epileptiform movements, and the electrical activity of the brain was profoundly disturbed. This state of affairs corresponds to the effects of anoxæmic anoxia produced experimentally by breathing an atmosphere of 8% oxygen or less, for ten to fifteen minutes (Davis *et al.*, 1938). Under these conditions, when the oxygen saturation in the internal jugular vein falls from the normal 65% to 28%, consciousness is lost and the EEG dominated by slow rhythms (Gibbs *et al.*, 1940). Thus, profound vascular hypotension produces an element of cerebral cellular anoxia comparable to that produced by marked anoxæmic anoxia.

It will be noted that the fall of B.P. was not accompanied by a gradual change of consciousness or cortical rhythm (Fig. 4). In the normal subject the systolic pressure was reduced from 130 mm.Hg

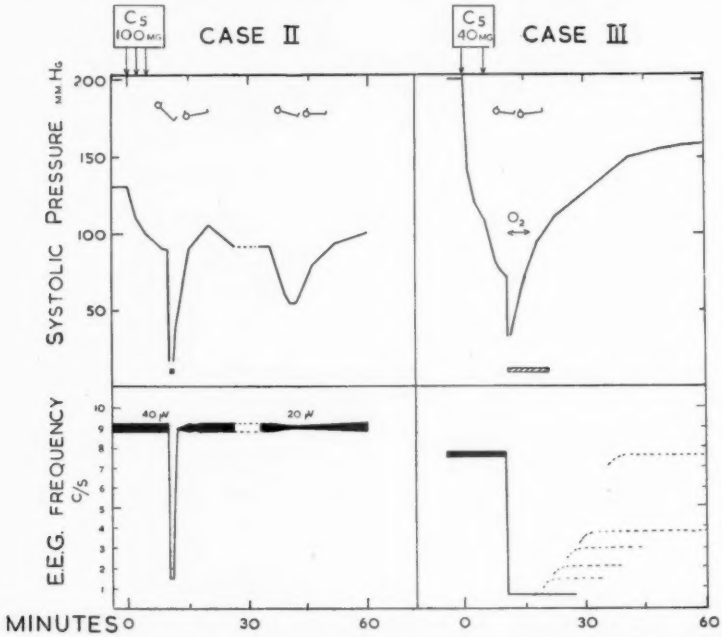

Fig. 4.—Comparison of Case II and Case III. Line figures at top of chart represent degree of tilt. Hatched rectangles under B.P. curves show periods of unconsciousness. In Case II the amplitude of the alpha rhythm is represented by the thickness of the line.

to 55 mm.Hg without any change of consciousness or electrical activity, and it was only at the latter level that a complaint of light-headedness and a diminution in the alpha rhythm gave warning that the cerebral circulation was becoming inadequate. In the arteriosclerotic subject, a proportionately greater fall of systolic pressure from 200 mm.Hg to 80 mm.Hg (but a comparable percentage fall of *mean* arterial pressure) produced no apparent change of cerebral activity, and it was not until the 70 mm.Hg mark was reached that the first signs of diminished electrical activity appeared. A further fall to 55 mm.Hg completely abolished consciousness and resting rhythm.

In both subjects changes of cortical activity had the quality of suddenness; the cortical rhythm changing from normality to gross abnormality over a narrow range of B.P. In the normal subject the upper limit of this range was 55 mm.Hg systolic, and in the arteriosclerotic about 75 mm.Hg.

The recovery of the two cases was very different. Whereas the normal subject (Case II) recovered rapidly and completely once the blood pressure rose above 50 mm.Hg, the arteriosclerotic subject showed a delayed recovery of consciousness and cortical rhythm, long after the B.P. had been restored to levels well above the point at which cerebral functions had first become disturbed.

Herein may lie the explanation of prolonged recovery times sometimes seen in patients submitted to controlled hypotension by means of posture and vasodilator drugs. It may be that cerebral anoxia, and not the anæsthetic drug, is responsible for the prolonged coma.

Summary

The electroencephalogram (EEG) has been used as an index of cerebral cellular anoxia in induced vascular hypotension.

Three conscious subjects were submitted to induced vascular hypotension by a combination of posture and a vasodilator drug. Continuous EEG recordings were made throughout the experiments.

In one subject the blood pressure failed to reach critical levels. In the other two subjects severe hypotension was accompanied by coma, convulsions, and profound disturbance of cortical rhythm. Recovery was prompt in a normal volunteer, but markedly delayed in an arteriosclerotic subject.

The significance of these findings is discussed in relation to ischæmic cerebral anoxia.

Acknowledgments

This work was carried out at Graylingwell Hospital, Chichester, and I should like to thank Dr. Martin Roth and his colleagues in the Research Department for their generous help and advice, and also the volunteers who made the investigation possible. I am indebted to Dr. G. Parsons Smith for reporting on one of the tracings.

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The Depression of Respiration by the Opiates and Its Antagonism by Nalorphine

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A new colour film entitled "Nalorphine" was shown by courtesy of the Wellcome Research Institution. The film demonstrated the action of nalorphine as an antagonist to morphine, methadone and thiambutene. A dog was shown deeply narcotized with morphine; nalorphine was injected into a leg vein and the dog woke up with startling rapidity—in twelve seconds he was sitting up and in half a minute he was running round.

All the effects of morphine are antagonized by nalorphine. The depressant effect on the respiration of a dog was shown to disappear in less than a minute. The effects on temperature were shown in rabbits: morphine alone produces a fall in temperature, if nalorphine is given simultaneously with morphine then there is only a very slight fall, comparable with that produced by nalorphine alone. The effect on gastro-intestinal propulsion was shown in rats: morphine alone causes a marked delay in the passage of food, nalorphine alone hardly any delay; morphine and nalorphine given together cause little more delay than nalorphine alone.

Methadone and its analogues, also pethidine and thiambutene share the actions of morphine and are antagonized by nalorphine. This was demonstrated on two animals, one narcotized with methadone and the other with thiambutene.

Respiratory depression I take to be a reduction in respiratory minute volume. This may be brought about in three ways: first, by a reduction in respiratory rate, the tidal volume remaining the same; secondly by a reduction in tidal volume, the rate remaining constant; or thirdly by a combination of both.

Under the conditions of modern anæsthetic practice the first two types of respiratory depression can be demonstrated quite distinctly. Pethidine, for instance, given intravenously in the doses usually used, causes a slowing of respiration, with little change in the tidal volume, while the barbiturates, represented by thiopentone, have little effect on the rate of respiration but reduce the tidal volume (Fig. 1). It is interesting to observe in Fig. 1 that although thiopentone produced a more profound

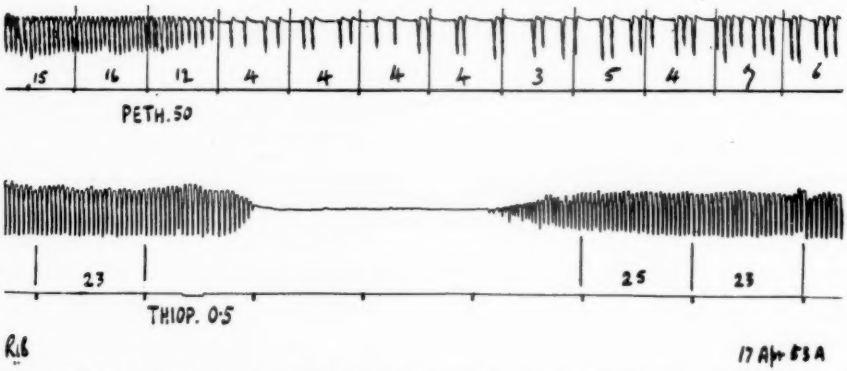


FIG. 1.—Effects of pethidine, 50 mg. (upper tracing) and thiopentone 0·5 gramme (lower tracing) on patients lightly anæsthetized with thiopentone and nitrous oxide. Tracings read L→R, inspiration downwards: figures indicate respiratory rate per minute.

depression, as apnœa persisted for two minutes, the minute volume was restored within five minutes; whereas the respiratory rate of the patient who received pethidine did not return to its previous figure for forty minutes.

These two types of respiratory depression may be tabulated thus:

TABLE I.—DIFFERENCE BETWEEN RESPIRATORY DEPRESSION BY 50 MG. PETHIDINE AND 0·5 GRAMME THIOPENTONE DURING ANÆSTHESIA

Respiratory characteristic	Pethidine	Thiopentone
Rate	Slowed	Not slowed
Tidal volume	Not diminished	Diminished
Minute volume	Reduced	Reduced
Duration of depression	Prolonged (20–30 min.)	Short (3–5 min.)

They are so distinct that one can hardly avoid concluding that they originate at different sites in the central nervous system, and consequently may be expected to be affected by different circumstances and drugs.

For the purposes of this paper I am calling pethidine an opiate. In fact my experience with making respiratory tracings of the effects of pethidine, morphine and papaveretum over the last three years has revealed no essential difference between them, except that for a corresponding depth of depression, pethidine has a shorter duration of action than the naturally occurring drugs.

The depressing effect of the opiates on the respiration may be demonstrated in three ways:

(1) By counting the respiration rate.

(2) By measuring the minute volume, e.g. with Gaddum's spirometer.

(3) By stimulating the respiratory centre with carbon dioxide.

(1) Counting the respiration rate demonstrates that the depressing effect of pethidine given intravenously during anæsthesia is influenced by the dose of papaveretum given for premedication. Each patient's respiration was recorded and the rate plotted as in Fig. 2. The average rate for five

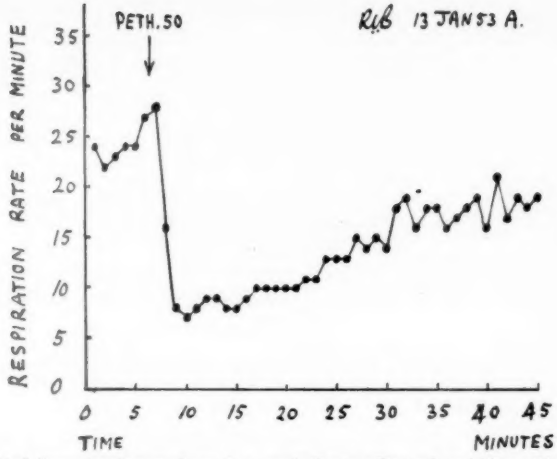


FIG. 2.—Graph plotted from tracing such as 1 a, to indicate effect of pethidine, 50 mg. intravenously, on respiratory rate. Note the slow return to normal.

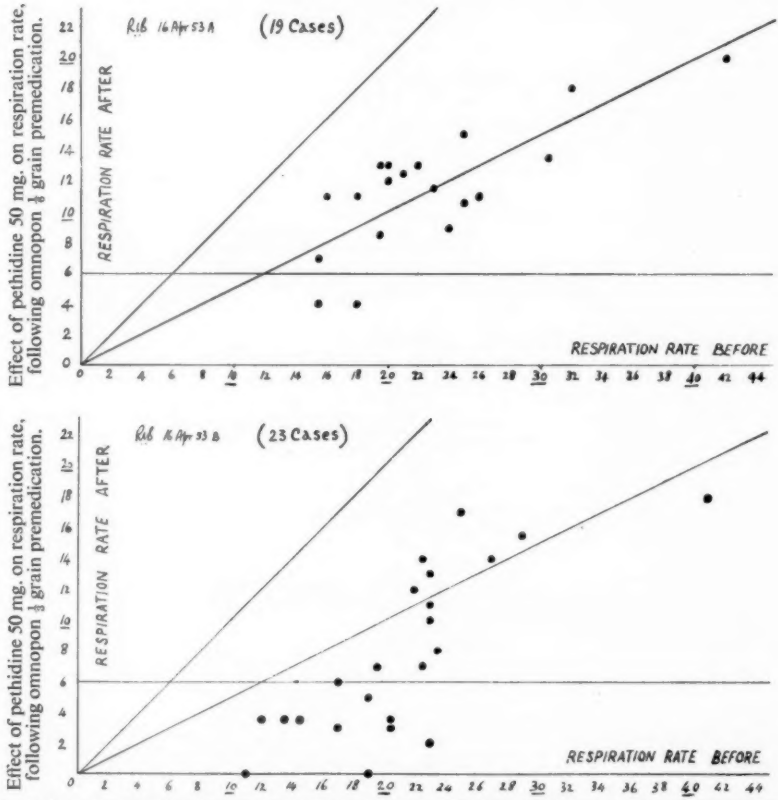

Effect of pethidine 50 mg. on respiration rate, following omnopon ⅓ grain premedication.
R.B 16 Apr 53 A (19 Cases)
RESPIRATION RATE AFTER
RESPIRATION RATE BEFORE
Effect of pethidine 50 mg. on respiration rate, following omnopon ⅓ grain premedication.
R.B 16 Apr 53 B (23 Cases)
RESPIRATION RATE AFTER
RESPIRATION RATE BEFORE

FIG. 3.—Effect of premedication on response to 50 mg. pethidine. Each point represents average rate for five minutes before pethidine plotted against average rate for slowest five minutes after pethidine. In each graph, upper diagonal is line of "no effect", lower diagonal indicates a reduction of respiratory rate by half.

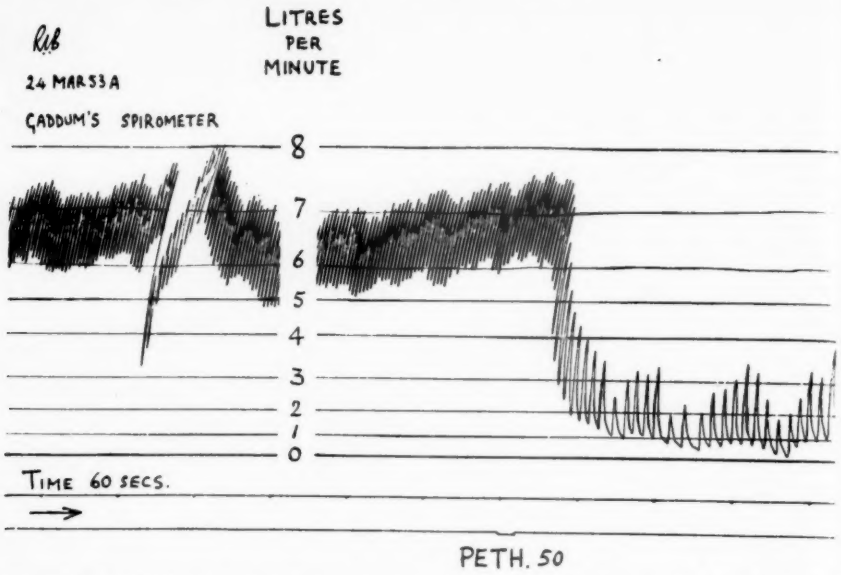


FIG. 4.—Effect of pethidine on minute volume as shown by Gaddum's spirometer. There is a profound fall from nearly 7 to less than 3 litres per minute.

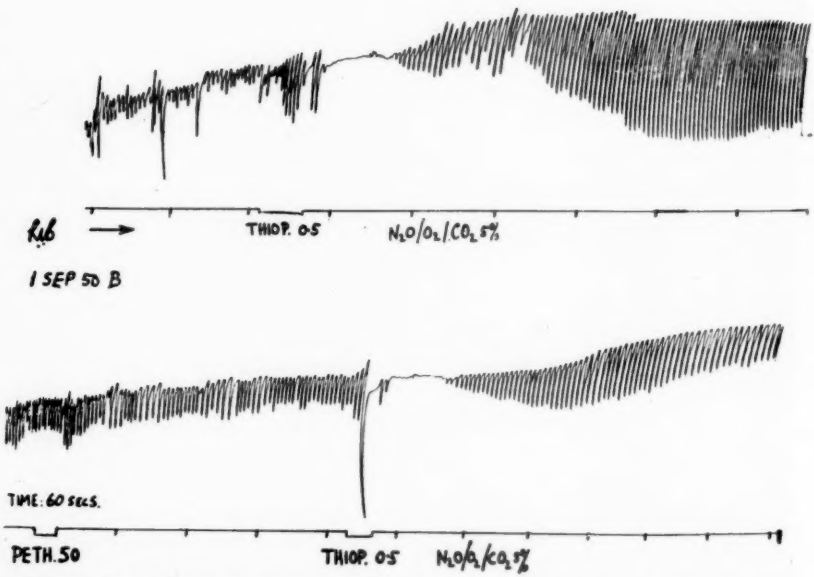


FIG. 5.—Effect of pethidine on the response of the respiratory centre to carbon dioxide. Upper tracing—control—shows great increase of respiration. Lower tracing—patient received pethidine—shows little response to same stimulus.

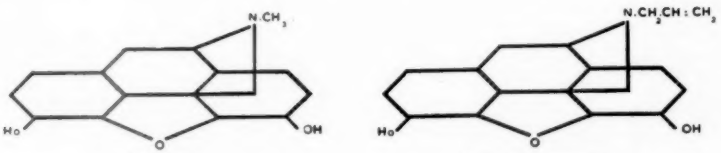
minutes BEFORE injection was then plotted against the rate for the slowest five minutes AFTER. Fig. 3 shows the results obtained in this way for two groups, the patients in the first group were premedicated with $\frac{1}{6}$ grain omnopon and in the second group with $\frac{1}{3}$ grain omnopon. Each patient was given 0·5 gramme thiopentone, 75% nitrous oxide and 50 mg. of pethidine. The depression of respiration after $\frac{1}{3}$ grain of omnopon is greater than that following $\frac{1}{6}$ grain. It is my impression that patients breathing at less than six per minute cannot maintain full oxygenation with 25% oxygen: if a line is drawn across at this rate it will be seen that only 2 patients of the 19 receiving $\frac{1}{6}$ grain omnopon come into this category, while 10 of the 23 receiving $\frac{1}{3}$ grain breathe at less than 6 per minute.

(2) Fig. 4 shows the effect of 50 mg. pethidine on the minute volume of a patient, using Gaddum's spirometer (1941).

(3) The effect of pethidine on the response to carbon dioxide is shown in Fig. 5. These tracings were made with a cuff round the chest and a Marey's tambour; they start with the patients awake. Each patient was given 0·5 gramme thiopentone, nitrous oxide, oxygen and CO_2 as indicated. The second patient was also given 50 mg. pethidine beforehand, this resulted in a much diminished response to CO_2.

Having defined respiratory depression and shown in various ways how it is brought about by the opiates, and, in particular, by pethidine, we can proceed to consider the new drug *N*-allylnormorphine.

N-allylnormorphine is now officially called nalorphine, it is available under the trade name "Lethidrone". Fig. 6 shows how similar is its structure to the morphine molecule. A methyl group



MORPHINE *N*-ALLYLNORMORPHINE

FIG. 6.—Outline diagrams of molecules of morphine and nalorphine.

is removed from the nitrogen, hence the term NOR from the German "Nitrogen ohne radicale". An allyl group is substituted (which really renders the NOR a misnomer). As might be expected from their similar structure the mode of action of nalorphine is believed to be a substrate competition for the same receptors that are affected by morphine.

In 1915 Pohl described *N*-allylnorcodeine as being able to antagonize the respiratory depression of morphine. *N*-allylnormorphine was synthesized by McCawley, Hart and Marsh in 1941. Unna carried out a number of experiments on dogs in 1943 and showed that nalorphine could rouse dogs anæsthetized with morphine.

Nalorphine seems to have been first tried in man for the treatment of morphine addiction: Wikler (1951) reported giving it to 12 post-addicts in whom it produced lethargy, mild drowsiness, vivid daydreams and dysphoria. In another paper, Wikler *et al.* (1952) reported that nalorphine produced the most intense abstinence syndrome ever observed in an institution for treating morphine addicts. Eckenhoff, Elder and King (1951) showed that nalorphine was effective in relieving respiratory depression due to morphine and pethidine during anæsthesia, but was ineffective against depression due to cyclopropane, ether and thiopentone: this is not surprising, as I have shown that the respiratory depression due to thiopentone at any rate, is of quite a different type.

During anæsthesia, nalorphine injected intravenously into a patient whose respiration has been depressed by an opiate restores the normal rate within half a minute. Fig. 7 shows the dramatic

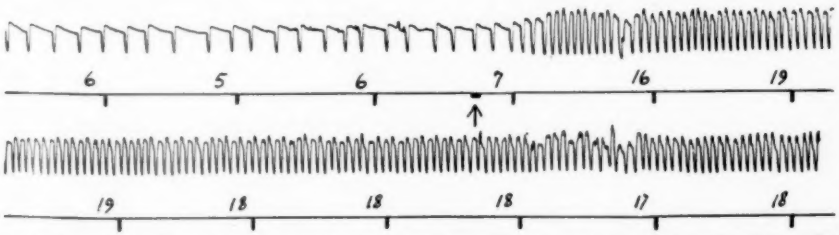


FIG. 7.—Effect of nalorphine (↑) on respiration depressed by pethidine. Tracings read L→R. Figures indicate respiratory rate per minute.

effect; the time marker indicates minutes and the numerals the respiration rate. The tracing reads from left to right: inspiration is downwards: the lower line follows after a delay of six minutes. There is no initial stimulation of respiration, but an abrupt return to normal rate, which is maintained. This contrasts with the effect of an analeptic, an example of which is Fig. 8, which shows the

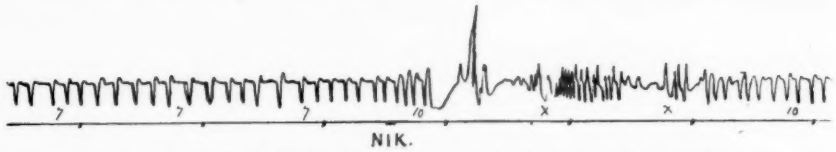


FIG. 8.—Effect of nikethamide (NIK) on respiration depressed by pethidine.

typical effect of nikethamide. Two ml. of this were injected into a patient anæsthetized with thiopentone, gas, oxygen and pethidine: the patient practically woke up, coughed,then settled down and carried on breathing at a rate of 9–10 per minute.

The effect of nalorphine on the minute volume can be seen in Fig. 9, using Gaddum's spirometer; this is the same case as Fig. 4, the minute volume is abruptly returned to normal.

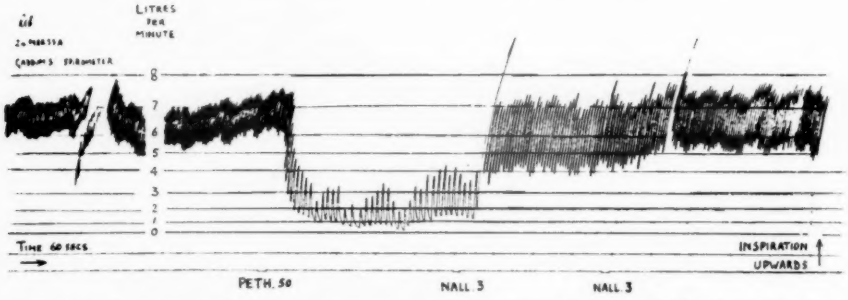


FIG. 9.—Nalorphine 3 mg. (NALL.3) reversing depression caused by 50 mg. pethidine. Gaddum's spirometer.

Having confirmed the remarkable antagonism of nalorphine for pethidine I attempted to determine the minimum dose necessary to restore the respiratory rate after a dose of 50 mg. of pethidine given intravenously. This was done by giving the pethidine and following it after five minutes with nalorphine given 1 mg. at a time at two-minute intervals, until no further increase in rate occurred. Fig. 10

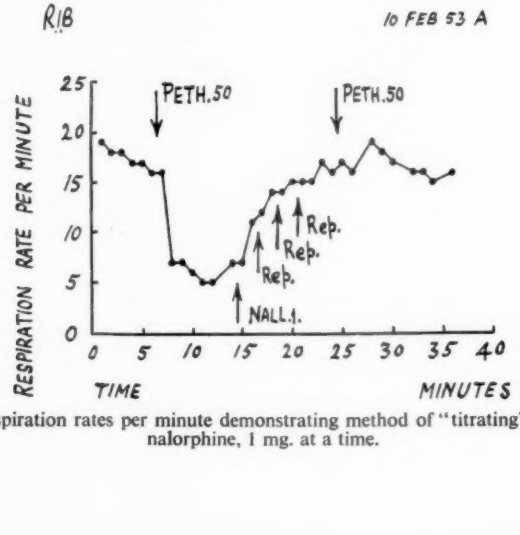


FIG. 10.—Graph of respiration rates per minute demonstrating method of "titrating" 50 mg. pethidine with nalorphine, 1 mg. at a time.

shows a typical result. Another point also emerges; a second dose of pethidine repeated after the nalorphine does not produce the characteristic slowing effect. It appears that nalorphine once established is not easily dislodged from the receptors for which it and pethidine compete. 3 mg. of nalorphine also restored the normal respiratory rate following the slowing caused by ½ grain omnopon intravenously.

Nalorphine is also reported to be effective against the other synthetic opiates—physeptone (Fraser *et al.*, 1952) and methorphinan (Chase *et al.*, 1952) as well as against the side-effects of morphine, e.g. hyperglycæmic effect and the increased activity in the bowel (Beal and Schapiro, 1953).

Up to the present, what may be called the morphine syndrome—pain-relief, respiratory depression, pin-point pupils and addiction—has remained indissoluble. But the appearance of nalorphine, a drug which completely antagonizes the respiratory depression, must lead one to consider whether a combination of drugs may not produce some pain-relief with a minimum of respiratory depression.

Fig. 11 shows the analgesic effect of pethidine as reflected in the respiratory pattern. A man was intubated for radical mastoidectomy with ½ gramme of thiopentone and 50 mg. of succinyl choline.

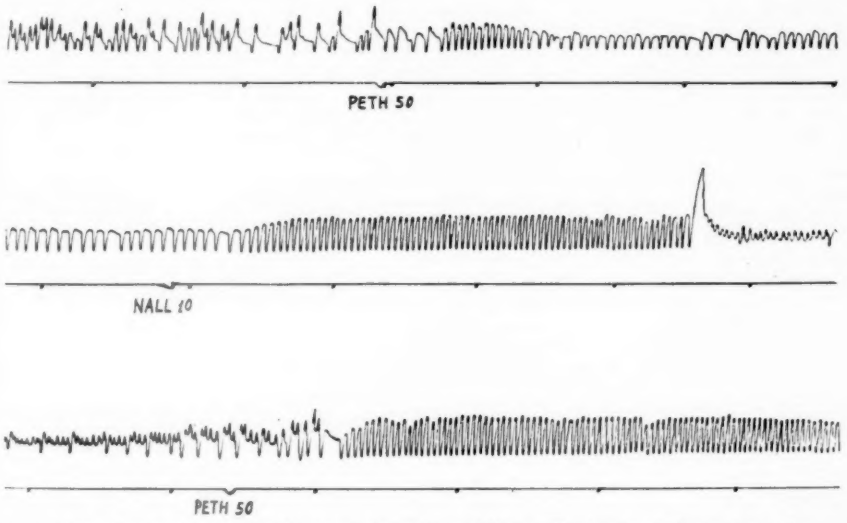


FIG. 11.—Effect of nalorphine on analgesia produced by pethidine. Tracing L→R from above downwards. Time: minutes. (*See* full discussion in text.)

Respiration returned and showed the irregular and hesitant form characteristic of a patient who does not tolerate an endotracheal tube. A dose of pethidine was given and the respiration changed to a regular form. An injection of nalorphine restored the rate to normal with no alteration in the rhythm at first, but after four minutes this suddenly reverted to the irregular character seen at the beginning. Finally, a second dose of pethidine was given, the respiration again became regular, but on this occasion no slowing took place. The surgical stimulus while this tracing was being made remained, to all intents and purposes, the same and consisted in the surgeon hitting the patient's head with a mallet and chisel: an exercise designed to try anyone's tolerance of an endotracheal tube.

There are three points to notice here. *First*, after the original dose of pethidine the respiration became regular before it slowed. *Secondly*, after the dose of nalorphine the respiration rate reverted to normal some four minutes before the surgical stimulus eventually broke through and set up the irregular rhythm again.

If we take the regularity of the respiration to indicate a measure of analgesia, we can infer that the analgesic effect of pethidine precedes the respiratory depression, as shown by the slowing of the rate. *Thirdly*, this is borne out by the effect of the second dose of pethidine which produced a regular rhythm at a normal rate.

Here, then, seems to be a possibility that the analgesic and respiratory depressing effects of the opiates may be separated. It may be that a carefully determined dose of nalorphine will antagonize the respiratory depression leaving a measure of analgesia. In order to test this, I have in a number of cases given 50 mg. of pethidine together with 3 mg. of nalorphine and obtained, I believe, some analgesic effect. This seems to me to be a line worth pursuing.

Now that there is an effective antagonist to the opiates the possibility of using sensory depression in place of muscular paralysis comes nearer achievement. The production of apnœa with very large doses of pethidine combined with hyperventilation may be used to replace muscle-relaxants. This would appear to be most likely in chest surgery, where relaxants are at present used not to gain access, as in abdominal surgery, but to keep the diaphragm still and to control the patient's tidal exchange.

The question of the use of nalorphine in midwifery is too large to embark on now; but there seem to me three ways in which its use might be explored. First, to give it some time before the opiates or pethidine so that it saturates the infant, *before* the mother receives her analgesia. Secondly, large doses of opiates may be given to the mother and their effect reversed just before delivery; or thirdly, the drug may be given to the infant after delivery as described by Eckenhoff, Hoffman and Dripps (1952). I have given doses of $\frac{1}{2}$ mg. to two infants delivered unexpectedly quickly after omnopon, with good results.

It occurred to me that we might be able to use larger doses of pethidine or morphine as a supplement to nitrous oxide in the casualty theatre, following them with a dose of nalorphine, before sending the patient home. Before doing this we decided to try the drug on ourselves; three of us each had 3 mg. intravenously. My two colleagues thought the word "dysphoria" did less than justice to their feelings. They sweated, shivered and felt sick and giddy for an hour after the injection and did not return to normal for nearly three hours. I had a feeling of heaviness in the head and felt slightly unsteady but this was relieved by undoing my tie. A sensation of unreality supervened for some time but did not prevent my eating a good tea half an hour after the injection. In view of the unpleasant symptoms experienced by my colleagues, I thought it hardly fair to give nalorphine to out-patients.

To summarize the uses to which nalorphine might be put I suggest:

(1) In the treatment of opium poisoning; including inadvertent overdoses to infants, the cachectic and shocked, and chronic bronchitic or emphysematous patients, who are particularly sensitive to the opiates.

(2) In the treatment of addiction.

(3) As an aid in the diagnosis of a patient with an acute abdomen who has ill-advisedly been given morphine.

(4) Combined with the opiates in midwifery—to the mother before delivery or to the infant after.

(5) As an aid to anæsthesia, allowing us to use the opiates more freely.

Summary

Respiratory depression is defined and the difference between that produced by the opiates and the barbiturates is illustrated by tracings from anæsthetized patients. The antagonism of a new drug, *N*-allylnormorphine, for the opiates is demonstrated. The possibility of producing analgesia without respiratory depression by a combination of drugs is discussed.

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A Historical Note on the Simple Dementing Form of Schizophrenia[1]

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CHANCE has recently brought to my notice a paper written by Arnold Pick of Prague in 1924, shortly before his death. In this paper, in which Pick concerns himself with some historical data from English writings on neurological and psychiatric topics, he devotes a chapter to the history of the simple dementing form of schizophrenia.

Pick had already dealt with the subject in a much earlier publication. In an article which appeared in 1891 he described in some detail the cases of three patients who fell under this denomination. The term in use at the time was primary chronic dementia (dementia præcox) of adolescent age. Pick drew attention to the fact that few references were to be found in psychiatric literature and especially in German writings, to that variety of the disease which is characterized by the unobtrusive way it begins in individuals, often of good intellectual endowment, who progress on the way to intellectual disintegration quietly, as he says, without dramatic clinical punctuations.

Reviewing the literature, he found relevant observations almost exclusively in French and English writings. These, for the most part, treated of the clinical material in question in terms of acquired or developmental idiocy. They comprise the names of Esquirol (1838), Rousseau (1857), Moreau (1859), Morel (1860) who introduced the term démence précoce, Falret (1876), Saury (1886), Legrain (1886), Langdon Down (1887), who, in his clinical description, went into greater detail than most of the other writers, Clouston (1888), Spratling (1889), Charpentier (1890) who spoke of "démence précoce simple des enfants normaux" and referred to earlier work by Bourneville. The only German writer in the series is Svetlin (1891) who, like Langdon Down, drew a rather more detailed picture of the disease-form.

It may be taken as a measure of the nosological novelty which the cases described by Pick represented at the time in the German psychiatric literature that his name has been eponymously linked with this form of psychosis. In the paper mentioned at the outset (Pick, 1924) Pick declines any such attribution to him of priority in the description of the simple dementing form of schizophrenia. He points out his earlier reference to the authors quoted in the article of 1891 and, thanks to an accidental discovery, he is able to add to the list one more name, the earliest in the series. It is that of John Haslam, the Apothecary to Bethlem Hospital, the same who first described general paralysis of the insane.

Pick had come across the second edition of Haslam's "Observations on Madness and Melancholy" printed in 1809 and it is from this that he quotes in translation, at full length, passages relevant to our subject.

As in 1924, when Pick was writing his article, so even to-day no references are to be found to this earliest record of clinical observation regarding the simple dementing form of schizophrenia, whether in textbooks of psychiatry or in works on history of medicine or, more especially, in works on history of psychological medicine. It may incidentally be remarked that the number of the latter is surprisingly few.

I will now quote this model of clinical description from the original (Haslam, 1809, p. 64):

"Connected with loss of memory, there is a form of insanity which occurs in young persons; and, as far as these cases have been the subject of my observation, they have been more frequently noticed in females. Those whom I have seen, have been distinguished by prompt capacity and lively disposition: and in general have become the favourites of parents and tutors, by their facility in acquiring knowledge, and by a prematurity of attainment. This disorder commences, about, or shortly after, the period of menstruation, and in many instances has been unconnected with hereditary taint; as far as could be ascertained by minute enquiry. The attack is almost imperceptible; some months usually elapse, before it becomes the subject of particular notice; and fond relatives are frequently deceived by the hope that it is only an abatement of excessive vivacity, conducing to a prudent reserve, and steadiness of character. A degree of apparent thoughtfulness and inactivity precede, together with a diminution of the ordinary curiosity, concerning that which is passing before them; and they therefore

[1] After a paper read at the Inaugural Meeting of the Epsom and Sutton Inter-Hospital Psychiatric Association at West Park Hospital, Epsom, on November 1, 1951.

neglect those objects and pursuits which formerly proved sources of delight and instruction The sensibility appears to be considerably blunted; they do not bear the same affection towards their parents and relations; they become unfeeling to kindness, and careless of reproof. To their companions they shew a cold civility, but take no interest whatever in their concerns. If they read a book they are unable to give any account of its contents: sometimes, with steadfast eyes, they will dwell for an hour on one page, and then turn over a number in a few minutes. It is very difficult to persuade them to write, which most readily develops their state of mind: much time is consumed and little produced. The subject is repeatedly begun, but they seldom advance beyond a sentence or two: the orthography becomes puzzling, and by endeavouring to adjust the spelling, the subject vanishes. As their apathy increases they are negligent of their dress, and inattentive to personal cleanliness. Frequently they seem to experience transient impulses of passion, but these have no source in sentiment; the tears, which trickle down at one time, are as unmeaning as the loud laugh which succeeds them; and it often happens that a momentary gust of anger, with its attendant invectives, ceases before the threat can be concluded. As the disorder increases, the urine and fæces are passed without restraint, and from the indolence which accompanies it, they generally become corpulent. Thus in the interval between puberty and manhood, I have painfully witnessed this hopeless and degrading change, which in a short time has transformed the most promising and vigorous intellect into a slavering and bloated ideot."

A modern table of classification of psychiatric diseases contains a dozen designations of categories and a large number of subdivisions. This list of classification, by no means yet completed, has evolved in a long process of differentiation, and integration, maintained by a drive for conceptual mastery of clinical experience, a drive which in its turn adds to the breadth and depth of the field of experience. At the time when Haslam wrote, this conceptual mastery could only be achieved to a rudimentary degree and for the rest an almost poetical vagueness had to suffice. On another page in his "Observations" Haslam writes: "Madness has many colours and colours have many hues." To him disorder of the mind, madness, was a unity. But, at the same time, his keen eye was discerning in the chaos which was the psychiatric scene of his day distinct clinical forms which to day are part of our psychiatric nosology.

Haslam's "Observations on Madness and Melancholy" (Haslam, 1809) appeared eleven years after the first edition of his work, published in 1798, under the title "Observations on Insanity". In this "corrected copy" the great psychiatrist—whose work, one is led to think, has not yet met with a just measure of appreciation—has enlarged his original "Observations" by "considerable additions which", as he modestly says, "the extensive scope of Bethlem Hospital would have furnished more liberally to a more intelligent observer". It is in one of these additions that he described for the first time what later came to be known as the simple dementing form of schizophrenia.

Bucknill and Tuke (1879) commenting on Haslam's priority in the description of general paralysis of the insane say that although "it would appear that Haslam first described the disease (he) did not name it. Calmeil who followed the English Psychologist gave it a name and got the honour of the discovery". One may conjecture that the identical circumstance, the lack of a differentiating name for the other disease form so classically drawn has played a part in keeping Haslam's merit in obscurity for more than a century.[1]

Since writing this historical note I have kept up my acquaintance with Haslam and I should like to use this occasion to put in on his behalf two further claims to priority.

The first concerns what we call to-day obsessional neurosis. This is a relatively new nosological entity, for the introduction of which into psychiatry we are chiefly indebted to Westphal. In his original paper which appeared in 1877 Westphal states that the earliest observations relating to this disorder of the mind can be gleaned from some of the case histories recorded in the writings of Esquirol. In this historical view Westphal is followed by Oppenheim (1923). Now, in Haslam's "Observations on Insanity" which, I may perhaps mention again, appeared in 1798, there is to be found on p. 132 a sentence which comprises the descriptive essentials of obsessional thinking. It is a reflective summing up of discerningly observed clinical material which reads: "It also does not infrequently happen that patients will declare, that certain notions are forced into their minds, of which they see the folly and incongruity, and complain that they cannot prevent their intrusion." We have here a descriptive definition of obsessional neurosis which to-day may be supplemented but cannot be bettered.

Haslam's other merit to which I wish to draw attention bears on the concept of manic-depressive psychosis. It is generally held that Jean-Pierre Falret and Baillarger were the first in modern times to put on record the alternation of recurrent attacks of mania and melancholia affecting the same sufferer.

[1]In view of the often misleadingly quoted bibliographical references in modern historical works to Haslam's description of the clinical picture of general paralysis of the insane, it may perhaps not be amiss to bring the exact data. The description first appeared in the "Observations on Insanity" (1798) on page 120. In the "Observations on Madness and Melancholy" (1809) it is found, enlarged, beginning on page 259. The expansive form of the disease is here described for the first time. The report of a case identifiable as that of general paralysis of the insane appears on page 64 in the 1st and on page 115 in the 2nd edition. It includes post-mortem findings.

The two French psychiatrists described their observations independently of one another in the same year, 1854, speaking of "folie circulaire" and "folie à double forme" respectively. From these beginnings is derived the development of clinical thinking which issued in the formulation by Kraepelin in 1896 of the concept of manic-depressive psychosis. Jules Falret is credited with the recognition in 1879 of the "mixed states" of manic-depressive illness. In his "History of Medical Psychology" Zilboorg (1941) says: ". . . both from the standpoint of terminology and clinical descriptions Kraepelin's nosological innovations were but the culmination of a generation of efforts in both France and Germany." But let us turn to Haslam. In the "Observations on Madness and Melancholy" he opposes the view of his contemporaries who considered mania and melancholia two different disease forms. Polemizing against this opinion he points out on page 33: " . . . for we every day see the most furious maniacs suddenly sink into a profound melancholia, and the most depressed and miserable objects become violent and raving. There are patients in Bethlem Hospital, whose lives are divided between furious and melancholic paroxysms. . . ." And further on: "It must also have been observed, by those who are conversant with this disorder, that there is *an intermediate state* (J. Z.'s italics), which cannot be termed maniacal nor melancholic: a state of complete insanity, yet unaccompanied by furious or depressing passions."

It is with Haslam that the line of modern psychiatric writers begins, to whom credit is due for contributions which are at the basis of our present-day nosological views regarding the group of manic-depressive psychoses.

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Jan Evangelista Purkyně

Czech Scientist and Patriot (1787–1869)

By HENRY J. JOHN, M.D., F.A.C.P.

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JAN EVANGELISTA PURKYNĚ, the noted Czech scientist and patriot, was elected to foreign membership of the Royal Society just over a hundred years ago, in 1850. His contemporaries in Britain were an illustrious group, including, among others, Sir Charles Bell (1774–1842), Marshall Hall (1780–1857), Thomas Addison (1795–1860), James Parkinson (1755–1824), Richard Bright (1789–1858), Lord Lister (1827–1912), Thomas Hodgkin (1798–1866), Robert Graves (1796–1853), William Stokes (1804–1878), Charles Darwin (1809–1882) and Thomas Huxley (1825–1895).

Perhaps at this juncture I should point out that Jan Evangelista Purkyně, prounced *Poor' keyn i e* in Czech, is the same man whose name appears as Johann Purkinje in English texts. If you pronounce his name as my American colleagues do, you call him *Per kin' je*, or sometimes *Per' kin je*. The spelling, Purkinje, is the phonetic approximation in German of the Czech name, but by the time this is rendered into English pronunciation, it becomes so garbled that no Czech, including the great scientist himself, would recognize it. In the material I have collected, I have found the name spelt nine different ways. These inconsistencies resulted from attempts to write the name phonetically on the

part of those unfamiliar with the Czech language. During Purkyně's lifetime, Bohemia was a province of Austro-Hungary, and the government exerted much pressure to Germanize the country and to suppress the native languages. Since all the officials and most of the priests were Germans whose knowledge of Czech, such as it was, was confined to the spoken language, the records kept during that period of births, marriages and deaths contained many incongruities in the spelling of the names. Germans do not differentiate clearly the pronunciation of *B* and *P*; hence these two letters were often interchanged. In the church record of Purkyně's birth, in 1787, the name appears as *Burkine*. In the same register, Purkyně's father was recorded as *Burkyne*, and in his death record, as *Burkynie*. In the records of Charles University, in Prague, during his student years, the name appears as *Purkinie* and *Purkinje*, again indicating the German influence. Still another spelling is *Purkynje*. Later, Purkyně signed his name by its correct Czech spelling in all his correspondence with Czechs, but used Purkinje during the years spent in Germany, and in his correspondence with those outside his native land. After he returned to Prague in 1850, he used only the Czech spelling, Purkyně.

Purkyně, who unquestionably is one of the great geniuses of science, had a phenomenal range of interests, as is demonstrated by the association of his name with various structures in anatomy, with visual and other physiologic phenomena and with numerous instruments he devised for his experimental studies. Although his name is familiar to every student of physiology and medicine, through the Purkinje cells, fibres, vesicle, network, figure, image phenomenon, kinesimeter, kinematograph, &c., these names in the medical dictionaries and texts give only a fragmentary idea of the scope and importance of his scientific contributions.

Surprisingly little has been published about his life and character, except in Czechoslovakia, in comparison to that which has been written about other scientific men of comparable stature. Only a few articles have appeared in the English language. One of the best of these is the short biographical sketch, published anonymously in 1870, the year after his death, in the *Proceedings* of the Royal Society. Whoever prepared this obituary must have been thoroughly familiar with Purkyně and his work, for it contains considerable detail and presents an excellent and unbiased tribute to him. The *Lancet* published a short piece about him in 1931, and on my side of the ocean, there have been articles in the *Journal of the American Medical Association*, in 1899, by Opitz, and in the *Scientific Monthly*, in 1929, by Robinson, besides the short sections that have appeared in various works on the history of medicine. Among the latter, the short discussion by Garrison, in his *Introduction to the History of Medicine* might be mentioned as an appreciative summary of Purkyně's contributions.

This neglect of Purkyně by English and European authors has probably resulted, in part at least, because many of his accomplishments were ahead of his time and hence were not properly appreciated by his contemporaries, and also in part because his work was sometimes purposely ignored by his confreres in Germany, where most of his important work was done, because he was an outlander, a Czech, who did not remain in Breslau to reap the praise and glory usually accorded to the ageing Professor Geheimrat, but instead returned to his native land to spend the last twenty years of his life. Even in Prague, despite his prominence and his great literary activity and public service until he died, in 1869, at the age of 82, there was surprisingly little study of his life, character and achievements until after the emergence of Czechoslovakia as a sovereign state following the First World War. During the nineteen twenties and thirties, numerous Czech authors explored various facets of his activities, and published considerable material on this remarkable man. In 1937, the one hundred and fiftieth anniversary of his birth, the number of publications on Purkyně reached a high point in Czechoslovakia, where the medical and scientific fraternity attempted to make amends for previous neglect of their illustrious native son. Since that time, the interest in him has continued, and new source material, including original notes and letters, is still being unearthed.

My interest in Purkyně dates back to 1909, when I was a medical student at the University of Kansas. Because of my own Czech origin, the name Purkinje, associated with the cell that is so designated, aroused my curiosity, and I decided to find out more about this countryman of mine who had left the imprint of his name in the medical literature. Since there was so little biographical material available in English, I began to explore the Czech sources, and thus became more and more familiar with the salient facts of his career.

After my service in the U.S. Army during World War I, I went to Prague, and set about gathering material on Purkyně, with the idea of writing a comprehensive biography of him, in English. I discussed my plans with my good friend, Jan Štenc, a publisher in Prague, and he was of great assistance to me in the collection of original source material, including photographs and correspondence. Afterwards, I made contacts in other European countries for procuring material on Purkyně; thus for thirty-five years, I have been accumulating a large mass of biographical and critical data concerning him. Most of the publications to date may be classified, for the most part, as source material, in Latin, German, Czech, French, English, Russian and Polish. Incidentally, Purkyně used all these languages, and also Greek, Italian, Hungarian, Serbian, Lithuanian and Danish.

Although the learned men of his generation had far more facility in foreign languages than is generally observed to-day, Purkyně was outstanding, even in his own time, in his ability to read and speak so many tongues. This facility was one indication of his superior capabilities which were developed, at least in part, by his association with the Piarist Order, as student and teacher, and from

living in various parts of Czechoslovakia during the early years of his life. The map (Fig. 1) shows the various places in which he resided.

German was the language used and the teaching of Latin was stressed at the Piarist Seminary which Jan Purkyně entered in 1797, when he was 10 years old. This Seminary was situated in Mikulov, in the southern part of Moravia. Before that, he had attended the elementary school, where the teaching was in Czech, in his birthplace, Libochovice. After his graduation from the Seminary, with training corresponding to that of a gymnasium, he entered his novitiate in the Order of the Piarist Fathers, with whom he spent three years, continuing his education and teaching at Stará Voda, Moravia; Strážnice, near the Hungarian border, and at Litomyšl, in Bohemia. It is often erroneously stated that he belonged to this monastic group, but he did not take the final vows, and hence was never actually a member of the Order. He received a release from the Father Provincial at the end of the teaching semester, in 1807, and then decided to dedicate himself to a scientific career. After leaving the religious order, he continued his studies for two years with the Philosophical Faculty at Charles University, in Prague. He then supported himself as a tutor, and later lived for three years at Baron Hildprandt's castle in Blatná. With the old Baron's help, he returned to Prague to study medicine during the years from 1812 to 1817. After his graduation, he remained in Prague another five years, as Assistant in Anatomy and Physiology at the University. In 1823, he was called to the University at Breslau, in Germany, to take the Chair of Physiology.

Purkyně did not marry until 1827, when he was 40 years old. His wife was Julie Rudolphi, the daughter of Professor Rudolphi, who taught Physiology at the University of Berlin. Although his wife was German, she learned the Czech language and shared his interest in Czech affairs and ideas. This congenial companionship was terminated eight years later by Julie's death and was punctuated by a series of tragic occurrences. Their two little daughters succumbed to scarlet fever, in 1832, and Julie's father died the same year. Two years later, in 1834, Purkyně's mother died, and the following year Julie herself contracted meningitis, which proved fatal. Purkyně was left with two infant sons; Emmanuel was 3 years old at the time and Karel but 11 months.

Despite these vital personal blows which came in such swift succession, Purkyně's work and teaching were carried forward without serious interruption, and publications on his scientific investigations continued to appear regularly during this period. After his wife died, in 1835, Purkyně applied for the vacant Chair of Anatomy and Physiology at the University in Prague, but the Austrian regime would not give him credit for the years he had spent in Prussia as Professor, and so he remained in Breslau. His tenure there lasted twenty-seven years, during which he established the first Physiological Institute in Europe and accomplished his most important scientific work. This portrait of Purkyně (Fig. 2) was made in 1837, when he was 50 years old and at the peak of his career as Professor of Physiology at the University of Breslau. Here his name has its correct spelling, in Czech. In 1850, when he was 63 years old, Purkyně was invited to return to Prague as Professor of Physiology, and by this time his

FIG. 1.—Map showing the various places of residence of Purkyně (1815–1866).

FIG. 2.—Lithograph portrait of Purkyně made at Breslau, in 1837, when he was 50 years old.

prestige was such that no bureaucratic obstacles were placed in the way of the appointment. Here he established a second Institute of Physiology, and continued to take an active part in the scientific, cultural, educational and political affairs of his native land until his death, in 1869.

To appreciate fully the measure of Purkyně as a man and as a scientist, it should be recalled that, besides the tragic circumstances of his family life which imposed on him the added difficulty and burden of rearing and educating two motherless sons, he had to cope with many frustrations and obstacles and prejudices created by the general political situation and by the unfavourable intellectual climate which surrounded him during the early years of his professional life. Nevertheless, despite his personal disappointments and sorrows, the lack of adequate facilities of space and equipment and the frequently unfriendly attitude of government officials and even of his own colleagues, he worked unceasingly on a tremendous variety of problems and produced new discoveries at a truly prodigious rate.

At the outset of his professional career, the intellectual life of the Universities in Germany and Austria was suffering under the pall created by the Carlsbad Resolutions, which were promulgated as law at the instigation of Metternich, in 1819, the year after Purkyně's graduation from medical school. The aim of this edict was to check the free expression of opinions in any way hostile to existing institutions and to ferret out and bring to justice subversive conspirators against the government who were supposed to exist in dangerous numbers. The provisions of these Resolutions, in effect, constituted a stranglehold on independent thinking and ideas among both professors and students, and created an atmosphere of fear and tension that was not conducive to healthy intellectual growth and development. Unfortunately, we have seen the same thing happen again in our own time.

Purkyně served as an Assistant in Physiology and Anatomy at the Medical School in Prague for five years after his graduation, and during this period began his research activities, and was a contributor to *Krok*, the first scientific periodical in the Czech language. He was also planning his future, and his aim was to devote his life to scientific medicine and to research. He applied for a teaching position, first in Prague, then in Budapest, in Graz and in Lubliana, but was not accepted. In those days it was difficult for a native Czech to become a professor, since Germans were preferred by the officials of the Austrian Empire. Purkyně became discouraged and planned then to become a private physician in the country, attached to some house of the nobility, and to devote his energies to the establishment of a school for gifted youths, along somewhat the same lines as that of Pestalozzi, the Swiss pedagogue, whose work he greatly admired.

He had just about abandoned hope of an academic post, when he received the offer to become Professor of Physiology at the University of Breslau, in the German part of Silesia. It was his doctor's thesis, "*Beiträge zur Kenntniss des Sehens in subjectiver Hinsicht*", first published in 1819, which gained him this recognition. This work had attracted the attention of the poet Goethe, who was interested in the same field of investigation. With his powerful influence and also that of Alexander von Humboldt, Purkyně was chosen for the post at Breslau, despite the opposition of the faculty there, who had chosen Franz Paul Gruithuisen, then Professor of Physics, Chemistry, Zoology and Anthropology at Munich, as their candidate. The attitude of these Breslau professors was that no one of outstanding ability would be coming out of Austria. After Purkyně's arrival in Breslau, this prejudice on the part of the faculty and administration found expression in various ways that created tension and added to the difficulties under which he had to work.

Because he spoke German with a slight Czech accent, Professor Otto, the Professor of Anatomy and Director of the Medical School, informed him sarcastically that if he wished to be understood by his students, he had better deliver his lectures in Latin. His methods of teaching also met with hearty disapproval. Purkyně was not content to repeat the theories of the old masters according to some classical compendium, as his predecessor, Professor Bartels, had done. He insisted on presenting practical demonstrations with his lectures, and in performing experiments on animals. These radical innovations were criticized by his colleagues as foolish idiosyncrasies and disturbing new-fangled notions. Furthermore, his requests for equipment and space to carry out his experiments were regarded as extravagant and unreasonable. He stirred up real trouble when he requested a modern microscope for his department, for the authorities could see no reason why a physiologist should need such an instrument. They sighed for the good old days of Bartels, who, after all, had become a famous Geheimrat and had been elevated to the Chair of Physiology at the University of Berlin, had written many books on natural philosophy, medicine and theology, had been able to diagnose all diseases in the most learned terms without any new gadget, such as Laennec's stethoscope, and yet he, the great Bartels, had never needed a microscope! The storm of outrage created by Purkyně's wish for a microscope was not easily quelled, and he did not procure the instrument until nine years later, in 1832.

Purkyně established his first physiological laboratory in an unoccupied corner of the college building which had been assigned to him for his work. This created another tempest, because to his colleagues, experimental work on animals appeared utterly useless and irrelevant, in connexion with medical studies. Moreover, Professor Otto, the Director, who was fastidious as well as officious, objected strongly to the stench. The situation created constant friction, and eventually Purkyně solved the difficulty by transferring the laboratory to his own home, where he lived and dined and slept in rooms

crowded with instruments and equipment and animals for experimental work, untroubled by the odours.

When viewed against this background of annoyance, frustration, criticism and personal tragedy, Purkyně's achievements during the early period in Breslau were truly amazing. The range and scope of his investigations were phenomenal, and he produced original discoveries—many of which had to be rediscovered much later by others—at a rate that seems almost impossible to believe. But Purkyně was an authentic genius and, as such, he knew what he was doing and had to do it in his own way and at his own speed, regardless of all obstacles that might arise to hinder him. He was a pioneer and trail blazer, both in his teaching and in his investigative work, and he opened numerous avenues of research in many special fields that have kept his successors busy down to the present day. His mechanical ability was outstanding, too, for he had to devise new instruments and methods for many of the problems he wished to explore.

In our present era of the subdivision of knowledge into multiple special fields, it is somewhat difficult to conceive how Purkyně could have made basic contributions in so many areas of investigation. This was partly due to the fact that he had the intellect of a genius which could not be limited to any one narrow field, and partly because the various special basic sciences were, in his time, just then emerging as entities from the broad general category of "natural philosophy". In fact, Purkyně himself was one of those who helped to lay the groundwork for later specialization by his insistence that scientific knowledge should be based on experimental observations rather than on theoretical speculations, and also by the fact of some of his discoveries which were basic to the development of new scientific disciplines. He is often credited, for example, with being the father of histology and of embryology.

The broad concept that Purkyně had of general physiology is evident from the manuscripts of some of his university lectures, which include mention of the following fields: (1) anthropology as the introductory science for physiology as a whole, (2) anatomy, (3) histology, (4) embryology, (5) the phenomenology of life, (6) physiologic mechanics, (7) physiologic chemistry, (8) physiologic dynamics, (9) physiologic psychology, (10) general physiology or the philosophy of nature ("Naturphilosophie"), (11) experimental physiology, and (12) applied physiology.

Gradually, through his exceptional attainments and his outstanding character, Purkyně began to be respected and to gain recognition in Breslau. Because of his interesting and unique methods of teaching, as well as his kindly and generous attitude, students were attracted to him, and many came from throughout Germany to attend his classes and work in his laboratory. Eventually his valuable services were acknowledged by his colleagues, and he became the "gemütlicher Österreicher" whose work was worthy of support by the University. Although it took him nine years to get his microscope, he later had less and less difficulty in acquiring the instruments and apparatus he needed. His small salary was increased to more respectable proportions and, in time, the Prussian Government erected a separate building for him, to be devoted exclusively to Physiology. This was the first Physiological Institute anywhere, and was opened on November 8, 1839. Forty years passed before a similar institute was established in Berlin.

At the time Purkyně reached his goal of a separate institute for physiology, he was 52 years old, and the fire of his genius had cooled somewhat. Although he continued his experiments—including those on himself—and his teaching and lecturing, he found that his increased administrative duties and responsibilities were incompatible with research, and in his later years produced less and less original scientific work. As someone has said, "It is pleasant to be a director or a dean, but who ever heard of a dean discovering anything?"

Purkyně's first investigative work was in the field of physiologic optics, and he continued his interest in various objective and subjective optical phenomena during his later career. The product of these activities is indicated in the terms, Purkyně's figures, Purkyně's images and Purkyně's phenomenon, and in the large number of later investigations that were stimulated by his keen, penetrating studies. His publications were, as a rule, short, but in a few paragraphs he set forth solid facts and germinal ideas that inspired other workers to pursue the problems and fill out the details. As Heidenhain has pointed out, Purkyně's publication "*Commentatio de examine physiologico organi visus et systematis cutanei*" contained many facts of basic significance, but these were overlooked or forgotten and had to be rediscovered by others many years later. For example, he described and illustrated in detail the pictures which result from reflection from the cornea and lens, and these were rediscovered by Sanson, in 1837. The latter merely described the reflection, but Purkyně had suggested that it be used for measurement of the curvature of the cornea and presented a method by which this could be done, thus providing a foundation for ophthalmometry. This suggestion of his lay dormant for seventeen years, when Kohlrausch first made use of it. In the same publication, Purkyně discussed the illumination of the human eye, showing its source and its significance. For this he used concave glasses, placed a light at a certain distance, and thus reflected the light into the eye of a dog. He thus discovered the principle of illumination of the ophthalmoscope, and made the invention of that instrument inevitable. He himself recommended using this principle of illumination in the diagnosis of eye affections, but it was twenty-four years before Ernst Brücke and Erlach followed this recommendation.

In the same lecture, in 1823, he described the use of oil on the skin and bright light for the study of the capillary network. Among his earliest experiments were those on himself, to study the effect of

various drugs, including emetine, opium, belladonna, stramonium, turpentine, ether, nutmeg, camphor and ipecacuanha. This was another phase that he kept up through the years, and even after he had become Director of his own Physiological Institute, he was nauseating himself with huge doses of digitalis in order to study the disturbances of vision. From 1820 to 1825, Purkyně also published several observations and experiments on vertigo, in which he analysed the effect of leading a galvanic current through the back of the head, the significance of the position of the head during movement, the effect of injury to the cerebellum, the corpora quadrigemina, &c. During these early years, he also began his work on embryology by discovery of the germinating centre in the hen's egg, which he studied before incubation and through various stages of embryonic development.

Purkyně must have carried on many experiments simultaneously, because a chronologic list of his publications contains reports on various and diverse subjects in the course of any given year. It is evident, though, that his interest in certain fields, for example, optical physiology, the effect of drugs, the function of the nervous system and sense organs, embryology and the structure of cells, was continuous, for he was constantly exploring new facets in these fields and making new discoveries which led him on to further investigation.

The name of Purkyně is probably best known in connexion with cellular anatomy, but it is not generally recognized that it was he who discovered that all living organisms, both plant and animal, are composed of cells, and that his report antedated that of Schwann, by two years. Purkyně was the first to grasp the significance of the cell as the elementary unit of organic composition and the first to emphasize the analogous microscopic structure of plants and animals. He explained that the plant cell differs from the animal cell merely in having a firm cellular membrane, which is often absent in the animal cell; he suggested that the animal cell be termed a "granule". Thus he stated the essence of the cellular theory which was elaborated by Schwann a little later. It was Purkyně also who introduced the term "protoplasm" into scientific literature. Interestingly enough, the selection of this term came about because of his early religious training. In an ancient manuscript by Venatius Fortunata (1530–1600) there was an old church song in which the first man, Adam, was described as created from "Protoplast". It was from this origin that Purkyně coined the word and used it for the first time in the scientific sense. Other terms which he introduced into the nomenclature were corpora amylacea, enchyma and cambium.

Purkyně presented the original descriptions of numerous types of cells, including bone, cartilage, certain muscular fibres, besides those on various nerve cells, for which he is well known. In 1837, when he reported his discovery of the ganglia cells in the grey matter of the brain, the cerebellum and the spinal cord, he described them as "central forms which are related to the elementary nerve fibres in the same way as central stations of power generators are to the conducting wires". He termed the ganglia cells "accumulators, manufacturers and expediters of the nerve power". The flask-shaped nerve cells with their axones and branching dendrites which form the middle layer of the cerebellum, as we all know, bear the name of "Purkinje." The "Purkinje" fibres which serve to produce autonomic contractions of the heart chambers and the "Purkinje" network of immature muscle fibres in the subendothelial tissues of the cardiac ventricles he also was the first to describe. He performed investigations on the finer structures of the arteries and veins, to determine the various layers and the arrangement of the elastic fibres. He studied the minute structure of the heart, delineating the fibrous structure of the cardiac muscle and pointing out the direction of the fibrillary bundles. He also discovered the fibrillary structure of the uterus. He revealed the presence of the gastric glands and also the sweat glands and their ducts.

In the field of functional physiology, Purkyně made many important contributions. He published investigations on the action of the heart, its mechanism and on the heart valves. He studied the cardiac movements in such a way that he was able to record them in their individual phases, on long sheets of paper, by means of the kinesimeter which he constructed. He then made an instrument which he called the kinematograph; this had a rotating cylinder and with it he reproduced the motion of the heart from his individual pictures. The principle employed in this device was the same as that which was later utilized in the development of cinematography. Purkyně was the first to call attention to the real origin of the suction action of the heart during diastole, and he supported this thesis with three proofs. The first of these was confirmed years later by Porter and Schmid, and the second by Chauveau and Fréderique; the third point was always generally accepted.

Another major contribution made by Purkyně, in collaboration with his pupil, Valentin, and published in 1835, was that on continuous ciliary movement. He recognized its significance and emphasized its ubiquitous presence in all animals and its independence of subjective or autonomous nervous control or of muscular influence. His work on digestion was also of basic significance. Besides his discovery of the gastric glands, he collaborated with Pappenheim, one of his students, in investigating the gastric secretion and its function. As a result of these studies, he expressed the view that the secretion of hydrochloric acid by the gastric glands is controlled by action of the nerves; Brücke rediscovered this years later. The experiments on artificial digestion included the demonstration of the dissolving power of acidulated pancreatic juice and the finding that mechanical movement and increased hydrostatic pressure speed digestion.

Purkyně measured the volume of air in breathing experiments by means of a simple spirometer

which long antedated that developed by Hutchinson. Another of his important observations was that hearing can be conducted through the bones of the skull, and he attempted to construct an apparatus, making use of this fact, that would aid the deaf. In this age of psychoanalysis, it is also interesting that Purkyně published a paper on the physiology of dreams, in 1821, and continued experiments on this subject much later, during his years in Breslau.

Francis Galton is usually credited with being the originator of fingerprint identification, but seventy years earlier, Purkyně had written: "The wonderful arrangement and design which are on the palm of the hand and upon the sole of the foot, and especially the little hollows on the fingertips, the papillary lines, command our attention." He then went on to describe with accuracy the unchanging character of fingerprints, which he illustrated with various configurations. His pioneer work is of value to all criminologists, and Major Arthur Griffiths, the British penitentiary inspector who wrote *The Chronicles of Newgate*, stated: "The permanent character of the fingerprint was first put forward scientifically in 1823 by J. E. Purkinje, an eminent Professor of Physiology, who read a paper before the University of Breslau, adducing nine standard types of impressions and advocating a system of classification which attracted no great attention." Thus, along with all his other achievements, Purkyně should also be honoured as the grandfather of dactyloscopy.

Besides the instruments already mentioned, Purkyně devised numerous apparatuses that have been widely used in scientific work. His name, of course, is associated with the kinesiscope, the kinesimeter and the kinematograph, in the medical literature. He also devised a goniometer, a microtome, a modified autostethoscope and numerous other instruments. He invented many procedures in microscopy technique. He constructed a dark-field ultramicroscope; he introduced various fixation methods, such as sublimate, acetic acid, alcohol; he was the first to study serial sections of tissue which he prepared with his microtome; he devised methods of intravital staining; he was the first to use Canada balsam; he introduced the Drummond limelight for the demonstration of microscopic preparations; he made the first photomicrographs.

Among the minor works from the long list of Purkyně's contributions might be mentioned his studies on dental structure; the contribution to acoustics, "*On Tartini's Third Tone*"; his auscultation experiment, by which he was able to determine the points of rest and motion of a vibrating plate, without employing Chladni's sand; his work on rhizopods, the nautilus and on the embryology of the tadpole; his original description of the peculiar formation of the skin of cucumber plants; his observations on the methods of fertilization in plants; microscopic studies on the circulation of plant juices.

Despite his prodigious productivity in research work, Purkyně did not limit his activities solely to the laboratory. He was greatly interested in teaching methods and was a principal pioneer in establishing modern methods in medical education. A statement of his own in regard to this is worth quoting: "The modern physician does not educate himself into a real investigator and physiologist in the clinic alone, nor by his study of the works of the old masters. His education, starting with the observation of the sick, continues in the laboratory, which is the proper environment for the teaching of science and the place where progress in contemporary medicine is made. Thus it is clear that it is primarily physiology, whose domain is laboratory experimental investigation, which is the peak of the education of a modern physician, the crown of his medical knowledge and the generator of all further progress. A physician must not delude himself that he understands disease just because he is able to name it and to classify it into a certain system, but he must know that he will understand disease only when he can cope with it scientifically, prognosticating as well as treating it. Such progress can be reached only by physiological research. Thus we see that physiology is the basic medical science."

Purkyně found time to take an active part in numerous cultural societies, both German and Slavic, during his years in Breslau. He often gave talks on his discoveries or some of his latest ideas before the *Gesellschaft für die vaterlandische Kultur* and the *Philomatische Gesellschaft*. He frequently served as president or patron of the various cultural organizations of the Slavic students in Breslau, and his home was a sort of unofficial consulate for this group. In addition, many Russians and Poles on their way to central and western Europe stopped in Breslau, where they were always welcomed at Purkyně's home.

Purkyně went to Germany because at the outset of his career, he was not able to secure a suitable academic position in his own land. During the twenty-six years that he spent in Prussia, which was the most productive and active period of his life, he participated in and contributed greatly to German cultural and scientific life. Nevertheless, he always remained in his own heart an exile and was forever devoted to Bohemia and to the Czech language and culture. For example, he translated poetry by Schiller and Goethe and other German writers into Czech, because, as he said, he wanted to demonstrate that the Czech language was just as satisfactory for expressing thoughts and emotions as any other language in the world. He derived great joy, also, when he found some of Komenský's manuscripts, which had been unknown previously, when he was travelling through Prussian Silesia, where Comenius (as Komenský is known outside Czechoslovakia) had spent part of his life as an exile.

Although on several previous occasions, when Purkyně had turned his eyes homeward and had attempted to obtain a position in Bohemia, he had been rebuffed and disappointed, finally, in 1850, his fame was so great that his native land was willing and ready to receive and honour him. A Czech

writer has reported that his return was celebrated not only in Prague, but in all the provinces. Purkyně was then over 60, and he had achieved renown throughout Europe, so he was no longer compelled to fight for a laboratory. The Austrian Government furnished him a splendid one, with a capable assistant, and an adequate salary. But the days of great discoveries were over for Purkyně, proving once more that fine buildings and apparatus alone do not produce new knowledge in science.

Nevertheless, it would be erroneous to believe that Purkyně's intellectual activity ceased, after his return to Prague, or that he entered into retirement there. He had already made enough discoveries to stimulate an entire institute of research in the study of various problems, and he continued his interest in teaching and other educational activities. He became active in Czech politics, and this alone, in the mid-eighteenth century, was enough to keep anyone busy. He was elected to the Senate and served with exemplary diligence. Purkyně devoted much time to writing in his later years; he translated much foreign literature into the Czech language and also some Czech works into German and other languages. He was the founder and editor of the *Journal of Natural History*, *Živa*, and for a number of years was one of its principal contributors. His popular essays stimulated great interest in nature and its phenomena. He was interested in various phases of psychology and in philosophical and other subjects. The *Journal of the Bohemian National Museum* was vitalized by his contributions. He continued to develop the ideas of Pestalozzi, the great progressive educator, and discussed the establishment of orphan asylums from a scientific standpoint and a school for geniuses. He pointed out the importance of eugenics to humanity, and discussed various scientific questions from the humanitarian viewpoint. The range of his interests was limitless, as is characteristic of the intellectual genius.

In everything Purkyně did or wrote, he displayed clarity of thought, thoroughness, purpose and perseverance. He had a dauntless spirit and was never afraid to enter into a controversy, no matter what the odds against him, so long as he was sure his cause was right. He was ahead of his time in many things, not only in his scientific work, but also in some of his ideas on education, politics and philosophy. Many of the ideas which he attempted to propagate a hundred years ago are now being studied and often accepted as new.

Although he was not always thoroughly understood by his contemporaries, Purkyně was greatly respected, admired and loved by his Czech confreres and countrymen. A year before his death, in 1868, the Bohemian Medical Society, which he had been instrumental in founding several years earlier, published a quarto entitled, "Quod bonum, felix, faustum fortunatumque sit, Joanni Ev. Purkyně, diem semisaecularem X. dec. 1868 summorum in medicina honorum in alma antiquissimaque universitate Pragena celebranti gratulatur. . . ." At his death, in July 1869, Purkyně was mourned by people of every class, in Bohemia. He was then in his 82nd year, and had retained his vigour of body and mind, despite a long and painful illness with kidney stones, to the last days of his life. Of him it may be said, as of Goethe and von Humboldt, he lived to complete his labours.

In this short presentation, it has been impossible to present any adequate idea of Purkyně's great mind and character. He was truly one of those great spirits who appear on this earth from time to time to show the rest of us what human beings can become. The range of his thought encompassed all the departments of life and his wisdom found expression in his scientific work, in his teaching, in his patriotic and political activities, and in his philosophical writings. His patriotism was not narrow or chauvinistic, but humanistic. As he once expressed it: "A nation is full of powers and strengths given by God to man, wherein they have their origin, their growth and their ending. In this manner nationality becomes a tree of life of all mankind, giving out three beautiful branches: religion, justice and sciences. All that is hidden in the depth of the spirit will blossom out."

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Section of Laryngology

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DISCUSSION ON HIATUS HERNIA AND ŒSOPHAGITIS [*Abridged*]

Dr. J. B. Harman: *The Symptoms of Œsophagitis.*

These are chest pain and heartburn. The first is similar to heart pains in its site and quality and is only to be distinguished by its frequency.

These symptoms are extremely common. They form part of the usual symptomatology of peptic ulcer, cholecystitis and pregnancy; occasionally they may be persistent and severe without other disease.

Table I gives the results of œsophagoscopy (Mr. York Mason) on 61 patients attending a general clinic in 38 of whom chest pains and heartburn formed prominent symptoms. The following deviations from the normal were found, all of which were at the lower end: Most advanced was a bright red velvety mucosa bleeding easily to the touch and showing one or more shallow ulcers sometimes surrounded by an inflammatory rim. Intermediate changes showed the same appearance, but without ulcers. The mildest consisted of a bright red velvety mucosa alone, which had no ulcers and did not bleed. It was concluded that this was, in fact, pathological and indicated inflammation. Over half of the 38 cases with symptoms showed changes. When it is remembered how sore a tongue or pharynx can be without visible inflammation it may be suggested that some of the apparently normal gullets were also inflamed. This preliminary investigation supports the view that chest pain and heartburn are caused by stimulation of an inflamed mucosa, and not by spasm or other mechanism. The usual irritant is reflux of acid. The degree of resistance of the mucosa to ulceration is as important as the irritant.

We may speculate on whether acid pepsin has anything to do with the *development* of inflammation, though it undoubtedly causes pain when it is there, and may alone be responsible for the unusual complications of deep ulceration and stricture formation.

TABLE I.—ŒSOPHAGOSCOPY OF 61 CASES

		Cases
Symptoms with œsophagitis		24
Heartburn	13	
Pain	17	
Both	6	
Symptoms without œsophagitis		14
Heartburn	11	
Pain	7	
Both	4	
Controls without symptoms		23
With œsophagitis	1	
Without œsophagitis	22	

Mr. Ronald Belsey: *Pathology and Treatment of Hiatus Hernia when Complicated by Œsophagitis.*

My observations are based on the study of some 250 cases, of which 200 were adults and 50 infants and children. These cases represent a selected group only in so far as all suffered symptoms sufficiently severe to take them to a doctor, or in the case of the children severe nutritional disturbance, and the majority were accompanied by some X-ray evidence of a hernia.

I shall not discuss the possible existence of an intrinsic sphincter at the lower end of the œsophagus, likewise I shall avoid discussion of the ætiology of the œsophagitis except to acknowledge the work of Wangensteen and his associates on the dramatic results of introducing gastric secretion into the œsophagi of experimental animals, and the more recent work of Aylwyn in correlating the incidence of œsophagitis with enzyme activity in the supra-diaphragmatic pouch of stomach.

Hiatus hernias can be classified into the uncomplicated and the complicated, the complications depending upon the anatomical type of the hernia.

The uncomplicated hernia can, and frequently does, cause symptoms sufficiently severe to induce the patient to seek surgical advice, and the more distressing symptoms are high epigastric or substernal pain and vomiting.

Of the common complications seen reflux œsophagitis and its sequelæ, fibrosis and stenosis, are the most important. The other complications are:

(i) disturbances of gastric function and a high incidence of acute lesser curve gastric ulcers causing hæmorrhage and perforation;

(ii) pulmonary atelectasis and fibrosis due to nocturnal regurgitation and recurring aspiration pneumonitis;
(iii) strangulation and gangrene of the stomach due to torsion or mechanical obstruction of the pylorus in types II and IIa hernias;
(iv) and finally, misdiagnosis and maltreatment.

We are concerned here particularly with the problem of œsophagitis. In the Frenchay Hospital series 57% of the adults and 75% of the infants and children were thus complicated. The diagnosis in each instance was based on œsophagoscopic findings, a routine method of investigation adopted in every case of hiatus hernia admitted to the hospital. In my opinion any diagnosis of œsophagitis based on X-ray evidence alone should be treated with considerable reserve. Mr. Brown Kelly will deal with the endoscopic features of this condition.

The predominant symptom of pain appears to bear little relationship to the presence of œsophagitis. Patients with the more severe degrees of this condition progressing to advanced stenosis of the lower third of the œsophagus, sometimes give a history of little or no pain at all. Dysphagia rather than pain would appear to be the symptom most characteristic of œsophagitis when it reaches the chronic stage.

My observations will be based largely on the examination of approximately 40 excised specimens removed to relieve severe dysphagia that could not be dealt with satisfactorily in any other way. The inflammation, which starts in the mucosa, spreads outwards to involve each coat in turn, till the whole wall of the œsophagus may be infiltrated with fibrous tissue and little evidence of the normal anatomical pattern can be detected on section. The mucosa may be hypertrophic or eventually destroyed and replaced by granulation tissue. The peri-œsophageal tissues are œdematous and hyperæmic and the mediastinal lymph glands are enlarged. The vagi become involved in the inflammatory tissue and may be unrecognizable to the naked eye. Below, the inflammatory changes stop short at the cardia; upwards, they extend to involve the whole of the lower third of the organ, but seldom more. What limits the inflammation to this region has not been determined. Gravity and the downward stream of saliva may tend to counteract the reflux and limit the extent of the inflammatory process. In the rare case of true congenital shortening with œsophagitis the subsequent stenosis is usually restricted to a very short segment of the œsophagus, and is seldom as severe as when the œsophagus is fully developed. The essential element in the inflammatory process is the infiltration of the normal structures with fibrous tissue; this leads eventually to the characteristic stenosis and secondary shortening of the lower third.

To what extent these changes are reversible is not yet known and the evolution of a rational approach to the question of treatment must await this information. The almost complete obliteration of the normal anatomy seen in many of the specimens suggests, however, that the damage is frequently irreparable. The rate of development of the fibrosis is difficult to assess as it is frequently not known how long the œsophagitis has been present. In children, extensive and advanced strictures have been seen to develop in a few weeks. That these strictures are not due to "spasm" or "œdema" alone has been demonstrated frequently by histological examination of the excised specimens. In adults, the history of dysphagia is often short and rapidly progressive, and more suggestive of malignant disease than an inflammatory lesion.

At this point I wish to stress the importance of mural fibrosis as a cause of dysphagia. This symptom may be so severe that no solid food at all can be taken, while at the same time a barium swallow may show a reduced but apparently adequate lumen.

Œsophagoscopy suggests the answer in revealing the rigidity and immobility of the stenosed segment. The œsophagus is not a mere duct between the mouth and stomach but a highly complex muscular pump, and any interference with its neuromuscular mechanism may render it quite incapable of passing on the bolus of food. One curious feature of the stenosis is that although it may reach an extreme degree it never becomes complete.

Treatment.—The proper treatment of chronic œsophagitis and its sequelæ is prevention—in short, reduction and repair of the hernia before irreparable damage to the œsophagus has occurred. It has been shown frequently that repair by a technique restoring a satisfactory sphincter to the cardia will lead to rapid healing of the œsophagitis. Once secondary shortening and stenosis have started adequate reduction of the hernia becomes progressively more difficult and unsatisfactory, but is usually attempted in the borderline case. I agree with Allison that true congenital short œsophagus is a rare condition, and that in the absence of chronic œsophagitis and acquired shortening the vast majority prove at operation to be reducible hernias. The term "congenital short œsophagus" is fortunately being used less and less by the radiologists.

When stenosis is advanced more radical measures are indicated. Endoscopic dilatation would appear to be contra-indicated so long as the mucosal ulceration is still active and, personally, I have had little success with this line of treatment, although it must undoubtedly be adopted in the case unsuitable for major surgery or where doubt exists regarding the severity of the damage to the organ. Furthermore, dilatation of the established stricture may temporarily relieve dysphagia but will at the same time facilitate further reflux from the stomach, and possibly lead to aggravation of the œsophagitis. I would venture the opinion that dilatation of œsophageal strictures can be a highly hazardous procedure, even in the hands of the experienced œsophagoscopist, and when oft repeated

in the case of a chronic stricture, the overall risk may be greater than that of a resection. In infants gastrostomy is sometimes called for as a life-saving measure and, provided the feeds are given as a continuous drip rather than intermittently, it may promote healing of the mucosal ulceration. Partial gastrectomy performed from below with the object of reducing gastric acidity is contra-indicated; it rarely achieves the desired object and may complicate an œsophageal resection that has to be performed subsequently.

In many cases resection of the lower half of the œsophagus followed by restoration of bowel continuity proves ultimately to be the only method of permanently relieving the dysphagia. The most satisfactory means of restoring bowel continuity remains a controversial subject. Allison excludes the stomach by closing the cardia and then performs an œsophago-jejunostomy by means of a Roux loop. Certain functional and nutritional difficulties may follow this procedure. Satisfactory results may be obtained by a modified œsophago-gastric anastomosis. If the whole stomach is retained and the œsophagus anastomosed to the fundus the risk of recurring œsophagitis at a higher level is considerable. However, when the upper half or pepsin-secreting portion of the stomach is resected along with the stenosed segment of the œsophagus, and a tube formed from the remaining portion of the greater curve is used for the anastomosis, this risk appears to be eliminated or considerably reduced.

Moreover, it has been found by trial and error that the higher the anastomosis the less the risk of further œsophagitis. I have performed this operation on approximately 40 cases with satisfactory functional results and, as yet, no evidence of any recurring œsophagitis at a higher level.

Mr. H. D. Brown Kelly: *Management of Hiatus Hernia and Œsophagitis.*

Œsophagoscopy is regarded as an essential part in the management of these cases, firstly to establish the diagnosis, to exclude the presence of malignant disease and to find out if ulcers are present, and secondly to carry out treatment by dilatation or other endoscopic procedure.

The œsophagoscopic appearances vary according to the degree of stricture and œsophagitis. On passing the upper sphincter, it is usual to find a somewhat dilated gullet with smooth walls and full of fluid. The fluid is sucked out, and as the tube passes downwards, it may be moved gently from side to side to assess the amount of dilatation. Regurgitation of gastric fluid into the œsophagus may be observed during the examination.

At a varying distance, but usually at about 30 cm. from the upper teeth in the adult, the gullet narrows to the rosette appearance of the cardia, through which in some cases the endoscope passes without much difficulty into the thoracic stomach.

In other instances a definite stenosis is encountered here, the lumen diminishing to perhaps 2 or 3 mm. in diameter. These cases are associated with a greater degree of dilatation of the viscus, food stagnation and œsophagitis. For several cm. above the stricture the œsophageal walls are smooth, red and velvety, and in areas covered with a whitish membrane. Small ulcers may be seen, and if touched with tube or sucker may set up troublesome bleeding.

With gentle, continued pressure, the tube may negotiate the stenosis which varies in length from 1 to 4 cm., finally emerging into a space obviously lined with gastric mucosa, the walls of which show rhythmical going apart and coming together with inspiration and expiration respectively. Occasionally a severe degree of spasm is encountered which prevents the tube or indeed even a fine bougie from passing the stenosed portion.

In children suffering from short œsophagus, it has been observed by some authors that if a swab of secretion is taken from the œsophageal wall and applied to litmus paper, an alkaline reaction is obtained, whereas a swab from the thoracic stomach is acid, thereby proving the presence of gastric mucosa with acid-secreting glands. My own experience has been that in most cases, and certainly in all my adult cases, the swabs from both œsophagus and thoracic stomach give a strong acid reaction. This is probably due to the free regurgitation of acid stomach contents into the lower œsophagus. In some instances there are also isolated areas of gastric mucous membrane in the gullet walls above the cardiac narrowing, which are responsible for acid secretion.

The normal gastric acidity in the infant is much lower than in the adult.

Some authors recommend the application of silver nitrate solution in strengths varying from 5 to 25% to ulcers in the lower end of the gullet. I have always hesitated to do this, as the presence of profuse secretion makes it impossible to confine the action of the caustic to the ulcer, and silver nitrate must be regarded as a strong irritant. It is preferable to treat the concomitant œsophagitis.

If a stenosis is present which is severe enough to prevent the passage of the endoscope, bougies may be passed but only under direct vision in the first instance. The utmost care must be taken to avoid injury, either by over-dilatation or by rough instrumentation. Injuries so caused can give rise to fresh ulceration, aggravation of the fibrosis and increased obstruction.

Some patients suffering from hiatus hernia with œsophageal stenosis may be kept comfortable by the passage of bougies at three- to six-monthly intervals over a period of years. Adequate medical treatment of the œsophagitis increases the time between instrumentation.

It has been commonly quoted that those who live by the bougie eventually die of the bougie, but the risk of perforating the stenosed short œsophagus is not so great as in the case of cicatricial stenosis

due, say, to swallowing corrosive. In the former, the narrowed lumen is usually centrally placed in the œsophagoscopic field, and not distorted or pulled to one side as is usual in the case of the latter. Again, the good results of dilatation in hernia cases are often due to separating the œsophageal folds glued together by inflammation and ulceration. This is a much less traumatic procedure than the rupturing of an annular scar.

At present I have a lady of 75, who for the past fifteen years has required bouginage every two months. She still has symptoms of œsophagitis despite medical treatment. Another patient, a youth aged 21, has had a bougie passed every month since the age of 12. He is really a case for surgery, but he refuses operation.

Treatment by dilatation is perhaps a partial admission of failure in treatment, as it means that there is a continuance of œsophagitis. When age, general condition or economic factors preclude surgery, the bougie has its place.

Development.—On viewing a section of the embryo, it is perhaps easier to understand the claims of those who maintain that the short œsophagus can be of developmental origin.

In the embryo of four to five weeks, the stomach is high up in the region of the neck. The distance to the pharynx is consequently very short, and the œsophagus is of minimal length. As the heart and lungs grow, the stomach descends, thereby causing an increase in length of the gullet.

The rapidity with which this occurs is shown by comparing a 4·9 mm. embryo with one of 7·5 mm. In the former, the junction of œsophagus and stomach is on a level with the bifurcation of the lung buds, while in the latter, not much more than a week older, the portion of gullet below the bifurcation almost equals in length the portion above this level.

Arrested development at the earlier stage can give rise to the short œsophagus and thoracic stomach.

Among the chief supporters of the view that fibrosis is the main cause of the short œsophagus is Mosher (1941). He maintains that the œsophagus can be infected before birth, and quotes 3 cases of newly born children, in whom narrowing of both pylorus and cardia was present. Fibrosis due to ante-natal infection was considered a more likely explanation than double spasm. Infection may be carried via the blood stream as an infective thrombophlebitis, or it may take place via the œsophageal glands.

That fibrous changes in the lower end of the gullet can take place at a very early age was shown in 1936 by A. Brown Kelly who demonstrated the condition in an infant of 6½ weeks old. The isolated areas of gastric mucosa in the œsophageal wall described by Taylor in 1927 are referred to in connexion with this ascending fibrosis. The islets occasionally ulcerate with a chronic inflammatory reaction which spreads up and down the gullet wall and is followed by fibrotic change in all the muscular coats, most marked in the plane between the longitudinal and circular coats.

Another factor in the production of stenosis is thrombosis of the superficial veins at the lower end of the gullet. Ulceration on to the surface of the mucosa then occurs. This ulceration causes the gluing together of the œsophageal folds producing a dysphagia which yields readily to the passage of a bougie.

Incidence.—Out of 12,000 gastric examinations carried out in ten years by the Radiological Department of the Victoria Infirmary, Glasgow, 170 revealed the presence of a hiatus hernia and short œsophagus. Of these cases, 30% showed demonstrable radiological evidence of œsophagitis, but a definite ulcer was only seen in 5 instances. Œsophagoscopic confirmation of the short œsophagus and thoracic stomach was obtained in 60 cases. All routine gastric examinations, and all those referred on account of œsophageal symptoms are now examined specially for hiatus hernia.

The short œsophagus in infancy and later life.—Some twenty-three years ago, I was present at the endoscopic examination of a number of children suffering from œsophageal obstruction in the Royal Hospital for Sick Children in Glasgow. These cases were published by Leonard Findlay and A. Brown Kelly in 1931 under the title "Congenital Shortening of the Œsophagus and the Thoracic Stomach Resulting Therefrom" (*see also* Kelly, 1930).

I often wondered what became of these children in after-life, whether they grew up into healthy men and women or whether their abnormality affected them in any way. An attempt was therefore made to trace them.

The endeavour met with partial success, as I have only been able to locate 6 out of the 9 recorded patients. 2, I find, have already been reported in 1949 by Rennie, Land and Scott Park.

One of these, a woman now aged 26, still has dysphagia and regurgitation, but is in good general health and served in the A.T.S. during the war. X-ray examination shows that there is a short œsophagus, thoracic stomach, and a partial stricture (Case VII)[1]. The second case, a male aged 23, shows a similar picture and also still complains of dysphagia, although he is sturdy and well built (Case IV).

Case I.—Boy, aged 2½ years when admitted to hospital in 1929 with the history of vomiting after semi-solid food for twelve months. Œsophagoscopy showed a dilated gullet full of frothy fluid. Marked narrowing at 19 cm. from upper teeth. The endoscope passed through this, and an easy view of gastric mucosa was obtained. Swallowing improved after instrumentation, but he required the passing of bougies at irregular intervals up to the age of 10 years. After leaving school he was a seaman for a time, and then served in the Army for four years, both at home and abroad. The Army diet did not upset him, and he suffered no gross indigestion. He occasionally experienced pain in the left side of the chest which he attributed to "wind".

[1] Case numbers are identical with Kelly (1930) and Findlay and Kelly (1931)

Case IV.—Male, aged 7 years when reported in 1930. There was a history of difficulty in swallowing since birth, which became acute one month before admission. X-rays and œsophagoscopy showed a short œsophagus with stenosis at 24 cm. and a thoracic stomach. He was treated with bougies over a period of two years. Now aged 30. Served for six years in the Royal Engineers, and had no trouble in swallowing. At present he works as a bus conductor and thinks that the irregular meals have caused a setback in his condition. Wind, indigestion and occasional regurgitation still trouble him.

Case V.—Girl, aged 11½ months when seen in 1930 with a history of vomiting since birth. Œsophagoscopy showed a stricture at 19 cm. It afforded no obstruction to the passage of the tube which passed readily into the stomach. The infant was treated by the passage of bougies twice weekly for 16 visits. Thereafter she remained well for over a year and then required readmission. Briefly, she had dilatation by bougie at irregular intervals up to the age of 9 years. She is now a bright, lively girl of 24, carrying out responsible duties as a secretary. Weight 9 st. 10 lb. Certain symptoms have persisted since childhood. Food must be finely divided to prevent sticking. Regurgitation while eating is frequent, a condition aggravated by emotional upset. Retrosternal pain also occurs. X-rays show a smooth œsophageal wall. The lumen of the distal half of the gullet is narrow and never opens up completely. There is no dilatation above the narrowed portion. No herniation could be detected in the Trendelenburg position.

Case VI.—Male, admitted at age of 14 months in 1930 with the complaint of vomiting since birth, Food was brought up during every meal, and rumination was a feature. Œsophagoscopy revealed the cardia at 15 cm., opening and closing with respiration. Beyond this narrowing gastric mucosa was encountered. After treatment with bougies, he went home swallowing well. He required readmission for dilatation on several occasions subsequently, but after the age of 9 no further treatment was necessary.

Now aged 24, he is a strong young man, who served in the Army, and for two years was in Malaya. Weight 11 st. 10 lb. Although there is no difficulty in swallowing, and no sensation of food sticking, he is fussy about his food. Certain symptoms persist. Retrosternal burning pain is frequent after a meal. Regurgitation is of daily occurrence, but he usually just swallows what comes up and continues eating. X-ray pictures taken in January 1953 show an œsophagus of normal length and patency, with well-defined mucosal pattern. No herniation could be detected through the hiatus in erect, prone or Trendelenburg positions. Stomach appears of normal size and shape.

The last 2 cases are of especial interest. In both a short œsophagus and thoracic stomach were demonstrated in early childhood both by X-ray and œsophagoscopy. Over twenty years later, despite persistence of symptoms, no evidence of thoracic stomach could be found on careful radiological examination, although Case VI still showed narrowing of the lower gullet. The fact that both still suffer from regurgitation and retrosternal pain shows that there is still incompetence of the valve mechanism at the hiatus and œsophagitis.

There is a possibility that in the long interval between examinations, the œsophagus has lengthened, the condition having been a delay rather than an arrest of development, and that the regurgitation is due to irreparable stretching of the structures at the hiatus by the thoracic stomach in infancy.

On the establishment of normal feeding, the weight of the loaded stomach may have helped in stretching the œsophagus.

On the other hand these patients may have sliding hernias, and the radiologist simply had bad luck in trying to demonstrate them, although all known methods of persuading the stomach into the thorax were employed.

All cases were treated by dilatation of the stenosed œsophagus, either by bougies, by the passage of the œsophagoscope, or by both. Treatment had to be continued at intervals up to the age of 10 years on an average.

Summary.—6 patients, 4 males and 2 females, who suffered from short œsophagus and thoracic stomach in infancy have been followed up after a period of over twenty years. All still complain of regurgitation or other symptoms of œsophagitis and incompetence of the cardia valve mechanism, whether a hiatal hernia is still present, or whether, as in two instances, none could be demonstrated. In the two latter, the gullets are of normal length, although one showed slight narrowing of the terminal portion.

Despite their complaints, the patients all led a normal, active life. 5 of them served in the Forces and made no attempt to evade service on account of their abnormality, of which they were well aware. General bodily development and growth, intelligence and mental activity seemed in no way impaired.

I have to thank Dr. D. C. Suttie, Superintendent of the Royal Hospital for Sick Children, Glasgow, for allowing me to quote the old case records, and Dr. K. Blum of the Radiological Department, Victoria Infirmary, Glasgow, and Mr. T. O. Howie for the figures regarding incidence.

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Mr. E. D. D. Davis said that the hiatus was a part of the respiratory mechanism like the upper sphincter, formed by the cricopharyngeus muscle; it prevented air entering the stomach during inspiration. The orifice of the œsophagus is closed at its junction with the stomach by the constrictor cardiæ and the folds of the mucosa.

The thoracic stomach and short œsophagus was a congenital abnormality and in many cases produced no symptoms until late in life.

Mr. John F. Lipscomb asked if Mr. Brown Kelly had considered doing a biopsy in his cases? It would be very interesting to know whether the mucous membrane was gastric or œsophageal at the lower end of what appeared to be the œsophagus.

Mr. Lipscomb preferred to think of these cases as reflux regurgitation with hiatus hernia, œsophagitis, ulcer and stricture as complications. In a personal series of 70 reflux cases which he had œsophagoscoped, hiatus hernia had occurred in about 51 cases. Œsophagitis as shown by mucosal change had occurred in about 28 cases. Biopsy in the early stages showed a round-cell infiltration, and occasionally in more severe cases a superficial ulcer, and in 1 case a very large ulcer. In some cases of advanced stricture there had been practically no history of dyspepsia or heartburn. It would be interesting to find out why this was so.

Mr. H. V. Forster said that he had recently seen again a patient whose first visit had been in February 1927. He was in very poor condition being unable to take solid food.

An original provisional diagnosis of cardiospasm was not supported at œsophagoscopy in November 1928 when a most resistant terminal œsophageal narrowing was assessed for its degree of resistance using with great care a Starks' mechanical expanding dilator with a rubber sleeve.

Recent X-rays showed an œsophagus which now at least was short, a terminal narrowing 4 in. below the level of the bifurcation of the trachea and then very well demonstrated folds of high-level gastric mucosa.

The patient was operated on in July 1953 by Professor Charles Wells. The stricture was dense and there was much peri-œsophagitis. A side-to-side anastomosis to a Roux-en-Y loop of jejunum was done and has proved very successful.

Though Mr. Brown Kelly had recorded some success from endoscopic treatment he (Mr. Forster) thought there was now little hope of giving relief by this route in his own case.

Mr. Ronald Belsey, in reply, said that he had learned a great deal about this subject from the papers written by Mr. Brown Kelly's father. He had been interested in his follow-up and in finding what had happened to these cases. One question was as to how long a patient could endure the horrors of dysphagia. Another thing which had impressed him was that obviously Dr. Harman, Mr. Brown Kelly, and himself were talking about different phases of the condition. He himself was dealing with a group of cases which, he was convinced, would never respond to any form of endoscopic treatment. There was nothing magical about the bougie, and he did not know what it was hoped to achieve by it. If one cut across the normal œsophagus the two ends would fly apart as a result of muscular retraction; the same retraction can explain the apparent shortening of the œsophagus when the ligaments between the cardia and the diaphragm are lax.

It was now understood that it was necessary in operating for hiatus hernia to anchor the cardia to the undersurface of the diaphragm, sometimes by a complicated technique, and it was that anchoring of the cardia which was the essential feature. Since the improvement in the technique in this respect the incidence of recurrence had gone down.

In speaking of pain he had meant substernal and epigastric pain.

Mr. Brown Kelly, also in reply, agreed that the cases referred to should be examined by œsophagoscopy to make the investigation complete. Unfortunately they had all been in and out of hospital since childhood, and while agreeing to be X-rayed, naturally objected to œsophagoscopy.

A biopsy was seldom required simply to establish the presence of gastric mucous membrane. The endoscopic appearances on entering the thoracic stomach were usually unmistakable. To punch out a piece of mucosa in the presence of regurgitated acid secretion might be followed by the formation of a chronic ulcer. Where there was any suspicion of malignancy biopsy was, of course, essential, but one should hesitate before traumatizing an inflamed œsophageal wall.

Mr. Belsey had condemned the use of the bougie. There were two types of hiatus hernia case in which the bougie was used. The first was that in which obstruction was due to the gluing together of the œsophageal folds by superficial ulceration. This responded readily to dilatation. The second type was the fibrous stricture. Here the passing of the bougie might be dangerous, but, as the narrowed lumen was centrally placed in the œsophagoscopic field, the danger of perforation was not so great as in the cicatricial stenosis due to corrosive. In the latter the gross distortion rendered bouginage more dangerous.

Section of Obstetrics and Gynæcology

President—A. C. PALMER, O.B.E., F.R.C.S., F.R.C.O.G.

[*April* 24, 1953]

DISCUSSION ON LESIONS OF THE INTESTINE AND OF THE URINARY TRACT RESEMBLING DISEASE OF THE FEMALE GENITAL TRACT

Mr. Lionel E. C. Norbury: There is often a marked resemblance between certain lesions of the intestinal tract and those of the female genital tract in their signs and symptoms. The outline of a mass in the pelvis, although involving the genital organs, may not be clearly defined. The portions of intestine which are commonly found in the pelvic cavity include the sigmoid loop or pelvic colon—the rectum—the cæcum and appendix, and certain coils of small gut, including the terminal portion of the ileum.

Lesions arising in any of these structures may, from the position of the affected viscus, simulate a lesion of the genital organs, or may secondarily involve these by adhesion or infiltration.

The differential diagnosis of lesions affecting the pelvic organs, both genital and otherwise, is assisted by a study of the clinical features of the case and the previous history. This should be followed by a general physical examination. Digital examination of the rectum is important as a routine investigation of a patient, especially if any abdominal lesion is suspected. Anatomical landmarks, particularly of the genital system, should be defined.

Many lesions may be found in the pouch of Douglas. When a mass is palpable in the pelvis, as evidenced by combined abdominal and rectal or vaginal examination, one naturally thinks first of lesions in connexion with the genital organs and then of disease in the other pelvic viscera including portions of the intestinal tract and vermiform appendix. Such a mass may be hard, suggesting a neoplasm, or soft, tender, and fluctuating as in the case of an inflammatory lesion or abscess. With the latter, the rectal wall may be œdematous, accompanied by excessive secretion of thin mucus due to associated proctitis.

Lesions of the intestinal tract which may simulate disease of the female genital tract:

The vermiform appendix.—Acute obstructive appendicitis in small girls with an appendix in the pelvic position may give rise to symptoms closely resembling those produced by torsion of the ovary or tube, as evidenced by right-sided abdominal pain of a colicky nature and acute tenderness or a tender swelling on rectal examination.

FIG. 1.—Gangrenous Meckel's diverticulum from an adult. It was adherent to bottom of pelvis.

A "pelvic abscess" of appendicular origin, as evidenced by a tender boggy swelling bulging into the rectum or vagina, may simulate a suppurating ovarian cyst or pus in the tubes, and give rise to confusion in diagnosis. Similarly peri-colic suppuration may be a sequela of diverticulitis or of carcinoma of the rectum or colon, with the formation of a pelvic abscess. A suppurating *Meckel's diverticulum*, forming a bag of pus hanging in the pelvic cavity and adherent to structures in the pelvis, is a further example.

Fig. 1 shows such a diverticulum removed from a patient upon whom I operated. The diagnosis was obscure. There was marked tenderness on rectal examination. The diverticulum was stretched and had the appearance of a gangrenous sausage about 5 in. in length.

A foreign body in the pelvis, such as a *swab*, may be discovered on rectal or vaginal examination. The clinical features are usually those of an inflammatory lesion, culminating in an abscess which may rupture into the rectum or vagina with extrusion of the offending body, thus settling the diagnosis.

Diverticulitis of the pelvic colon may produce a large left-sided abdominal mass simulating an inflamed adherent ovarian cyst. This usually occurs in middle-aged or elderly people.

When I was Surgical Registrar at St. Thomas's Hospital I was called to see a patient who was being operated on for a supposed tuberculous ovary. The opposite ovary had been removed previously for "tuberculous disease". When I arrived in the theatre, the abdomen was already open and the mass proved to be in connexion with the sigmoid colon. I diagnosed the condition as a carcinoma, and was kindly invited by the gynæcologist

to proceed. With much trepidation I resected the affected portion of bowel and did an end-to-end anastomosis: the patient recovered. The specimen was examined by the late Professor L. S. Dudgeon who said he had never met with such a pathological condition before. The tumour was not a carcinoma but was an inflammatory mass showing an abundance of fibro-fatty material surrounding small pouches of bowel-wall; in other words a condition we now know as diverticulitis. This was in the year 1907 or 8. Unfortunately, being very junior, I did not publish the case. A year later, Telford of Manchester published the first recorded case in this country of diverticulitis of the colon.

A few months ago, your President operated upon a patient with a left-sided pelvic tumour, suggesting an adherent inflamed ovarian cyst. An exploratory incision revealed a mass in connexion with the pelvic colon, apparently a malignant growth, and adherent to the uterus. He closed the abdomen and kindly asked me to take over the case.

On abdominal exploration, I found a lesion of the pelvic colon. The diagnosis lay between a carcinoma and diverticulitis with an inflammatory mass. No enlarged lymph nodes were evident, and no lesion of the liver demonstrable. I was inclined to the diagnosis of diverticulitis and performed a local resection of the bowel with end-to-end anastomosis. The patient made a good recovery.

Pathological examination revealed "localized diverticulitis with much fibrosis and abscess formation in the wall of the colon" (Fig. 2).

FIG. 2.—Diverticulitis of colon.

FIG. 3.—Torsion of great omentum in hernial sac.

It is not unusual for "diverticulitis of the pelvic colon" to simulate a left-sided inflamed ovarian cyst.

A carcinoma of the pelvic colon may also produce a palpable tumour resembling an inflamed adherent ovarian cyst. It may be difficult to determine the site of origin of a growth involving both the rectum or pelvic colon, and the uterus. The vaginal wall and even a coil of small gut may form part of the malignant mass, and there may be hæmorrhage from both vagina and rectum.

A carcinoma of the rectum or pelvic colon or a diverticulitis of the colon may be followed by a *recto-vaginal* or *colo-vaginal fistula* with the passage of fæces *per vaginam*. Again a recto-vaginal or colo-vaginal fistula may result from ulcerative colitis, or from tuberculous disease of the rectum or vagina.

Segmental colitis, sometimes described as "Crohn's disease of the large bowel" may form a palpable mass resembling certain lesions of the female genital tract, especially when the bowel is adherent to the uterus or tubes. Segmental colitis may be found in patients who have no lesion of the small bowel. It resembles a colonic form of Crohn's disease, with patchy ulceration of the mucosa and fibrosis of the bowel wall, forming a definite tumour.

I had a case of *segmental colitis* in a woman, in which some 6 in. of the pelvic colon were involved in an inflammatory lesion, simulating regional ileitis as described by Crohn. I removed an enlarged lymphatic gland from the adjoining meso-colon, for diagnostic purposes, and this proved histologically to resemble a tuberculous lesion.

Volvulus.—The differential diagnosis of a volvulus of any abdominal organ may at times be a difficult problem owing to a similarity of the symptoms at onset. The symptomatology of volvulus of the small gut, cæcum or pelvic colon may simulate a twisted ovarian cyst, especially if the affected loop of bowel is adherent to the ovary. Or again a volvulus of the great omentum may also come into the picture. Fig. 3 shows a volvulus of the great omentum which was adherent to a hernial sac.

Inflammatory conditions of the small bowel such as "regional ileitis" or tuberculous disease of the small gut, in which the affected coil has become adherent to the back of the uterus, may be mistaken for a degenerating fibroid or inflammatory lesions of the tubes or ovaries. Fig. 4 shows a stricture at both the proximal and distal ends of the affected portion of ileum.

FIG. 4.—Regional ileitis. Inflammatory mass involved appendix. (Mrs. B., aged 36.) *Segment of ileum:* The specimen consisted of the terminal 8 in. of the small intestine. The wall of the bowel was much thickened and had lost its normal elasticity. Dissection showed a tubular stricture about 4 in. in length towards the distal end of the ileum and also a smaller stricture half an inch in diameter situated about 1 in. from the proximal end. At its distal end the bowel was acutely kinked, forming a band bound down by dense adhesions. *Microscopic structure:* Sections through the region of the stricture show the typical histology of regional ileitis. There is no sign of tuberculosis or of neoplasm.

Incidentally, *regional ileitis* (or Crohn's disease) and *tuberculous enteritis* may be followed by fistulous communication with the vagina. Crohn's disease, a granulomatous lesion of unknown origin, is characterized by great thickening of the bowel wall involving some portion (usually the terminal part) of the ileum and forming a definite tumour.

A degenerating fibroid may be mistaken for an inflammatory mass of omentum in the pelvis of appendicular or intestinal origin.

Some years ago, I was confronted by this difficulty in the case of a doctor's wife who was several months pregnant, and showed signs of an acute abdominal lesion with a tender pelvic mass thought possibly to be of appendicular origin. At the operation I found a degenerating uterine fibroid, which I enucleated. The patient went to term, and was delivered of a fine female infant.

Sarcoma of the rectum. In the non-ulcerating type, rectal examination will reveal a hard mass involving the rectal wall but with the mucous membrane intact, and thus unlike a carcinoma.

The rare *rectal endometrioma* is also certain to cause mistakes in diagnosis.

One must also bear in mind that a firm mass, or multiple areas of induration, palpable in the pouch of Douglas on rectal or vaginal examination, may be the result of so-called trans-colonic spread from a carcinoma of the stomach, or possibly the colon.

Lesions of the Recto-vaginal Septum

Recently I saw a patient aged 48, complaining of severe pain in the perineum. A small tender mass could be felt on both rectal and vaginal examination, apparently arising in the septum, and involving both the rectal and vaginal walls, but with intact mucous membrane. Biopsy *per vaginam* proved the lesion to be a "*transitional cell carcinoma of an anaplastic type*", possibly derived from some vestigial structure in the recto-vaginal septum such as misplaced epithelium of the rectum or anal canal. A similar case was operated upon at St. Mark's Hospital by H. E. Lockhart-Mummery recently. [The specimen shown included the rectum, uterus and vagina.] *Such a tumour has some affinities with the mucus-secreting carcinomas which occur in fistulous tracks, and are characterized by a malignant growth outside the rectum, with no visible primary tumour in the rectum.*

Inflammatory Stricture of the Rectum

This may be extrinsic in origin, the result of fibrosis following radium treatment for cancer of the cervix. I had such a case with marked fibrosis involving both the rectal and vaginal walls resulting in a very tight stricture of the rectum. This was followed by symptoms of acute intestinal obstruction necessitating a colostomy. After some months of systematic dilatation of the stricture, the colostomy was closed.

Lymphogranuloma inguinale may be responsible for the development of a rectal stricture in women. This venereal infection primarily involves the posterior vaginal wall, producing what is called the genito-ano-rectal syndrome with marked fibrosis and stricture formation.

Injection of piles with *sclerosing fluids* may, at times, be followed by a marked reaction resulting in a hard indurated mass or ring.

I call to mind a lady whose piles I injected with a 5% solution of phenol in almond oil. When she came to see me a week later I found an extensive hard submucous mass, involving both the rectal and vaginal walls. A gynæcological colleague who saw her suggested at once that the mass was due to my injections.

Double Lesions.—It is, at times, difficult for a patient to be certain as to whether blood is coming from the vagina or rectum. "*Bleedings*" from below, especially when they come from two places simultaneously, may give rise to confusion. For example: hæmorrhage from a rectal polyp associated with bleeding from a cervical polyp. Independent malignant growths of different histology may involve two organs simultaneously, such as the pelvic colon and cervix uteri. Such a case was that of a woman aged 48, who had a very large mass of fibroids and was suffering at the same time from increasing intestinal obstruction. Your President became suspicious, because fibroids do not usually cause intestinal obstruction, although their presence is often associated with some degree of flatulence.

Sigmoidoscopy, which is of value in doubtful cases of intestinal obstruction, in this case showed marked constriction of the pelvic colon at a distance of 18 cm. from the anus. At operation, after dealing with the fibroids, he investigated the colon and found a "ring carcinoma" in the lower part of the pelvic colon, the cause of the obstruction. He kindly referred the case to me. It was found possible to resect the growth and restore continuity of the colon.

Again, extensive rectal prolapse may be associated with complete uterine procidentia.

Sigmoidoscopy is important in the differential diagnosis of lesions resembling disease of the female genital tract. Narrowing of the lumen of the bowel may suggest diverticulosis. The openings of diverticula may be visible. Also, it may be possible definitely to establish the presence of a carcinoma of the rectum or pelvi-rectal region.

Mr. E. W. Riches: Gynæcological lesions overlap with urological conditions even more than they do with intestinal affections; both the symptoms and the signs have much in common.

Symptoms

Bleeding.—Hæmaturia is a sign of malignant disease in more than 60% of cases. A woman takes less notice of bleeding than a man and she often assumes that the bleeding is uterine. She may even deceive her doctor into making the same mistake so that the gynæcologist to whom she is sent must be constantly on his guard. Even a urethral caruncle will be missed if the urethral orifice is not inspected, and on this score there is a great advantage in using the cystoscopic position. A carcinoma of the urethra is even more serious although those which involve only the anterior urethra or its orifice have a good prognosis and can often be cured by irradiation (Riches and Cullen, 1951). The deeper growths and those which involve the bladder as well are much more malignant and may give rise to widespread metastases.

When there are no abnormal gynæcological signs to account for bleeding it is often advisable to cystoscope the patient. One woman who still bled after dilatation and curettage then had a hysterectomy. When bleeding again recurred she was sent for cystoscopy and her papilloma of the bladder was cured by cystodiathermy. It seems remarkable that a woman of average intelligence should not recognize hæmaturia, but it happens commonly.

A single woman of 55 was sent to a women's hospital on account of intermittent vaginal bleeding which had continued for a year. Full examination not being possible in the out-patient department she was admitted for examination under anæsthesia. When a catheter was passed blood-stained urine was withdrawn, and cystoscopy showed an extensive necrotic papillary carcinoma for which total cystectomy was performed by my colleague Mr. I. H. Griffiths. Another similar patient had undergone dilatation and curettage at a women's hospital two years before the true diagnosis of carcinoma of the bladder was made by cystoscopy.

Vesical bleeding can also occur from less serious lesions, such as a ureterocele, which can be destroyed by cystodiathermy, thus saving the kidney from progressive hydronephrosis.

Vaginal discharge even without bleeding is a common feature of urethral new growths; sometimes it is caused by a simple polyp.

Increased frequency of micturition in women is one of the conditions which the two specialties are often pleased to exchange. Urethro-trigonitis may exist without urinary infection but there is often an associated inflammatory condition of the genital tract which is equally difficult to cure. Ainsworth-Davis (1950) has written: "The characteristic symptoms of frequency, dysuria and backache, usually with a sterile urine, are almost invariably due to a chronic cervicitis in women who have borne children." The repair of a minor degree of cystocele has usually little effect, but if there is a serious genital lesion its removal or treatment will sometimes cure the frequency.

A woman of 25 from Iraq had frequency, suprapubic pain and diminished menses for ten years. She had previously suffered from tuberculous peritonitis, paratyphoid and amœbic dysentery. Laparotomy abroad had disclosed a mass in the right broad ligament, adherent to the bladder, which was also fixed to the uterus. It could not be removed and sections were indecisive. After the operation she started to have hæmaturia which was more copious at each period.

The cystogram showed an indented filling defect on the dome of the bladder.

Cystoscopy disclosed a vascular mass of œdematous tissue on the back of the bladder; cystoscopic biopsy, which was repeated, showed only chronic inflammatory changes. A mass was felt in the right side of the pelvis. A course of emetine had no effect, and I still suspected an endometrioma, despite the negative biopsy. With the assistance of a gynæcological colleague, Mr. Ian Jackson, the pelvis was again explored. The mass was a distended tube and cystic right ovary; the uterus was firmly adherent to the bladder and was removed with a piece of it. Sections showed chronic ulceration with tuberculous giant cells. She made a complete recovery, the relevant part of her history being the tuberculous peritonitis.

Incontinence of urine may be of the stress type for which so many different operations have been devised. For my part I prefer the one described by a gynæcologist, Mr. Everard Williams (1947). True incontinence is more commonly due to a urological cause and whilst the ectopic ureter opening into the urethra or vagina is somewhat of a rarity its occurrence must be remembered. The patient whose pyelogram is shown in Fig. 1 had undergone two operations by a gynæcologist to tighten the

FIG. 2.—Bilateral pelvic ectopic kidneys causing a pelvic tumour.

FIG. 1.—Pyelogram of ectopic ureter arising from upper half of right "double kidney" and opening into the urethra. Incontinence cured by heminephrectomy. Reproduced from *J. Obstet. Gynæc. Brit. Emp.* (1937) **44**, 517.

ure[illegible]ral sphincter; the supernumerary ureter opened into the urethra and she was cured by her[illegible]nephrectomy and removal of that ureter (Winterton, 1937). In another case the additional ure[illegible] opened just behind the urethral orifice. It was treated by my colleague Mr. I. H. Griffiths by [illegible]mplanting the extra ureter into the bladder.

Retention of urine in women is not common in urological practice as both stricture and neurogenic lesions are rarer than in men, and a woman has the great advantage of never suffering from an enlarged prostate. Patients with an impacted fibroid causing retention are occasionally sent to a urological clinic and require hysterectomy or myomectomy.

Signs

The *physical signs* which sometimes cause confusion are those produced by abdominal or pelvic tumours. When a kidney is very large, and especially if it is cystic, it may be mistaken for an ovarian cyst, and I have been called upon to remove a large hydronephrosis after a colleague had done a laparotomy for a suspected ovarian cyst.

A new growth in a normally placed kidney should not be confused with a genital tract tumour, but where the two co-exist a mistake may be made.

A woman of 40 had left renal pain and was found to have slight hydronephrosis on that side. She also had uterine fibroids and it was thought that they were obstructing the left ureter; accordingly a hysterectomy was performed. Shortly afterwards hæmaturia commenced and cystoscopy disclosed papillary growth of the bladder. During the next fifteen years she underwent repeated treatment by cystodiathermy, which culminated in the removal of her left kidney for pyonephrosis; it contained papillary carcinoma. The growths in the bladder persisted and it became necessary to do a total cystectomy and left ureterectomy. The whole ureter was packed with papillary carcinoma and there were multiple tumours in the bladder, a condition unlikely to be relieved by hysterectomy. She survived for a further three years before dying of multiple metastases in the lungs. Full urological investigation in the first place would have given the correct diagnosis.

A pelvic ectopic kidney is in a different category from the normally placed one; although the condition is sometimes bilateral (Fig. 2) it is not infrequently the only kidney present and its conservation is of extreme importance. The presence of two functioning kidneys can be determined by pre-operative investigations. Intravenous and retrograde pyelography are the most useful, but the final determination may rest on aortography which shows the vascular supply to the ectopic kidney and its absence on the other side. When two kidneys are present a knowledge of the anomalous blood supply to the ectopic one is of great help should it have to be removed.

FIG. 3.—Pyelogram showing deviation of the ureter produced by a retroperitoneal cyst.

In my experience *retroperitoneal or perirenal tumours* have caused more uncertainty than renal tumours.

A woman of 50 had a large tumour in the right side; the gynæcologist who did a laparotomy found it to be retroperitoneal and not ovarian. A subsequent intravenous pyelogram showed a non-functioning right kidney with a mottled shadow in the loin. I removed an ossifying fibroma weighing 5½ lb. She remained well for five and a half years when there was a large local recurrence; this time it was a solid spindle-cell sarcoma weighing 7½ lb. and I had to remove the right half of the colon with it. Despite X-ray treatment she had another recurrence eighteen months later from which she died.

A woman of 21 was found to have a smooth firm swelling in the left lower abdomen. Pyelography showed that it displaced the ureter inwards and forwards (Fig. 3); it was a simple mucus-secreting retroperitoneal cyst which shelled out easily (Fig. 4).

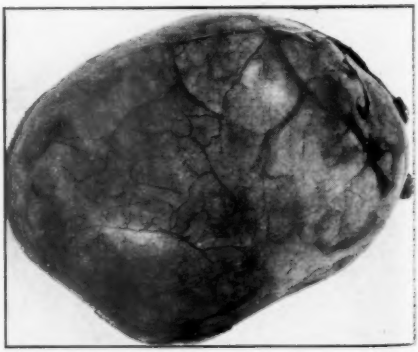


FIG. 4.—The cyst removed in the same case as Fig. 3.

A nurse of 49 noticed a lump in the left lower abdomen; thinking it was ovarian she consulted a gynæcologist who found it was not in the pelvis and sent her for urological investigation. The pyelogram showed the ureter displaced laterally by the tumour. At operation it was found to be a solid retroperitoneal sarcoma surrounding the common iliac artery, and it was necessary to resect 2 in. of that vessel. Removal was followed by X-ray treatment and she remains well and working four years later. An aortogram taken after three years showed an efficient collateral circulation.

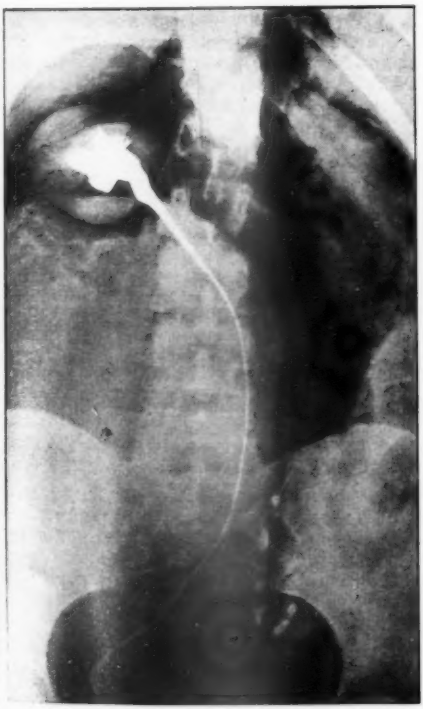
In these cases use has been made of the ureter in differentiating between a retroperitoneal and an intraperitoneal tumour. I do not think that such deviation is ever produced by an ovarian tumour. There is another method of diagnosis available, the retroperitoneal insufflation of oxygen. In the case shown in Fig. 5 such a large tumour was obviously sent to a gynæcologist first; it proved to be a retroperitoneal lipoma weighing 4 lb.

There is more excuse for misdiagnosis in the case of swellings in the true pelvis. A bladder full of growth or of urine is occasionally a source of error. When the bladder is fully distended it is often asymmetrical and in some such cases it may be justifiable to make the diagnosis by passing a catheter as the textbooks tell the students. A diverticulum of the bladder is a rarity in women, although a traction diverticulum following a vaginal hysterectomy is not unknown, and it may contain a stone formed around a nucleus of silk.

There is sometimes confusion even with the orthopædic department; because a woman had a pain in the back she was sent to an orthopædic hospital. They did a routine X-ray and found a shadow which was thought to be a large bladder stone. The bladder was empty at cystoscopy and the shadow was a calcified fibroid.

Finally there are the swellings in the vagina. I have mentioned those due to carcinoma of the urethra but there are also the soft vaginal cysts which may come to either department. It is worth while doing a urethrogram as some of them are really diverticula of the urethra (Fig. 6).

I think the main lesson to be learned from these borderline cases is the need for pre-operative investigation. An intravenous pyelogram will often clarify a doubtful situation and a cystoscopy



G. 5.—Large retroperitoneal lipoma shown by ography and perirenal oxygen insufflation. ureter is displaced medially and forward.

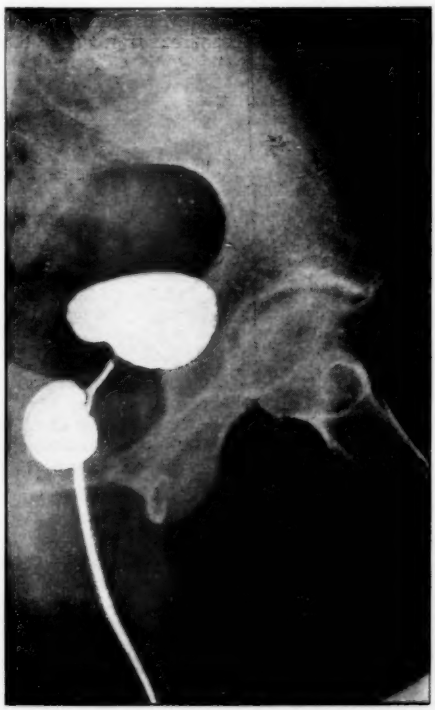


FIG. 6.—Diverticulum of the urethra simulating a vaginal cyst (cysto-urethrogram by D. W. Lacey, F.R.C.S.).

will, at least, determine whether there is a growth in the bladder. If there is, the patient should be sent on; the choice of treatment for bladder growths is often difficult and demands very full investigations. The worst possible treatment is exploratory cystotomy. Whoever opens the abdomen should be prepared to deal with whatever he finds there, but if he knows what he is going to find his task will be easier.

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Mr. Douglas MacLeod: There are many conditions of the urinary and intestinal tracts which are likely to resemble gynæcological lesions. Errors in diagnosis occasionally are unavoidable, and under such circumstances gynæcologists may be called upon to undertake some form of genito-urinary or intestinal surgery. All gynæcologists should be competent to deal with simple bowel resection and anastomoses, some will be capable of dealing correctly with major intestinal procedures, but those who are not so practised should call in the aid of a surgeon if he be available, or failing this leave the condition untouched and close the abdomen.

Lesions of the intestinal tract are more often diagnosed as gynæcological conditions than are those of the genito-urinary tract. A pelvic kidney may be mistaken for a fibroid, but this must be very rare and its only importance lies in being able to recognize it, especially as the kidney may be the only one. A large hydronephrosis also may simulate an ovarian cyst, but this also must be uncommon. On the other hand it is certainly not uncommon for a gynæcologist, on opening the abdomen, to be confronted with an unsuspected intestinal lesion. These will usually be found affecting the distal alimentary tract, and lesions of the upper alimentary tract are not likely to be a common cause of error. A diverticulitis or carcinoma of the sigmoid, pelvic colon or of the pelvi-rectal junction may be easily mistaken on pelvic examination for a fibroid or even a malignant ovarian tumour. Further, a diverticulitis or carcinoma of the colon may be associated with a pericolic abscess and simulate a large pyosalpinx. In many of these cases a careful history would suggest the possibility of such a condition and would indicate sigmoidoscopy and X-ray investigation, but certain tumours which do not occlude the bowel may give no suspicion of an intestinal lesion. Three cases of my own illustrate this point, and incidentally were all found to have tumours affecting the upper alimentary tract.

The first was an elderly patient complaining of pain; and pelvic examination disclosed a smooth tumour which I took to be a fibroid undergoing degeneration. Laparotomy revealed a tumour the size of a large orange attached to the antemesenteric border of a loop of small bowel. On section it proved to be a neurofibroma (Fig. 1).

The second case was a woman with an enormous abdominal swelling which I considered to be an ovarian cyst. Laparotomy, however, showed a tumour springing from the greater curvature of the stomach which on section appeared to be a myxosarcoma. Four years later the patient was admitted to Westminster Hospital and Mr. J. K. Morrison informed me that the condition had recurred (Fig. 2).

The third case was also diagnosed as an ovarian tumour, but laparotomy disclosed a large tumour affecting the small bowel and its mesentery and necessitating resection of 18 in. of the gut. Section showed it to be a sarcoma and the patient died of recurrence two years later (Fig. 3).

Endometriosis may give rise to symptoms closely resembling other surgical conditions. It not uncommonly affects the intestinal tract and also the urinary tract to a lesser degree. The fact that the symptoms are most noticeable at the times of the menstrual periods and the patient, who is usually in the middle thirties, is either childless or at least has not had a child for some years, should suggest the diagnosis. It is a condition which is dependent on active ovarian secretions and therefore is never seen before puberty and disappears spontaneously after the menopause.

Ovarian endometriosis is one of the commonest forms, which may be felt as a tender fixed lump in the pelvis. It presents usually as the chocolate cyst which tends to perforate. If the perforation is sudden, chocolate material escapes into the peritoneal cavity and signs and symptoms exactly resembling an *acute* appendicitis may be produced. Secondly, it is not uncommon for endometriosis to affect the small and large bowel. It may be associated with pelvic endometriosis but may also occur alone. When affecting the small bowel the lesion is usually to be found in the last 12 in. of the terminal ileum. A history of attacks of pain and vomiting occurring at the times of the menstrual periods would be strongly suggestive. These attacks increase in severity until acute intestinal obstruction results. As it is usually impossible at laparotomy to distinguish the condition from a carcinoma resection is the correct treatment for all cases.

The sigmoid colon is not an uncommon site and may be affected either by direct invasion by an endometrioma of the overlying ovary or the condition may occur primarily in the bowel without any pelvic endometriosis being present. The symptoms are, again, attacks of pain occurring at the

menstrual periods, but severe intestinal obstruction is rare. The treatment again is resection unless the diagnosis is certain when it can, on occasions, be locally excised. If the patient is over 40 a bilateral oophorectomy is all that is required providing no obstruction is present.

Though a barium enema in those cases might show some occlusion of the bowel lumen, sigmoidoscopy would reveal a healthy mucous membrane.

Endometriosis of the rectum, affecting it in varying degrees, is not uncommon and in advanced cases may closely resemble a carcinoma and indeed not a few abdominoperineal excisions have been performed for this reason. The condition is usually associated with an extensive endometriosis of the recto-vaginal septum which may in some cases erode the epithelium of the posterior vaginal fornix (Fig. 4). Some degree of obstruction will occur at the times of the menstrual periods and as

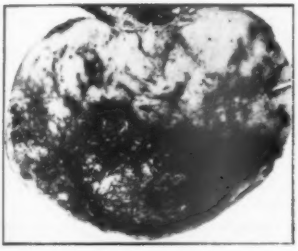

FIG. 1.—Cut section of neurofibroma of small intestine.

FIG. 2.—Myxosarcoma of stomach.

FIG. 3.—Retroperitoneal sarcoma affecting the small bowel.

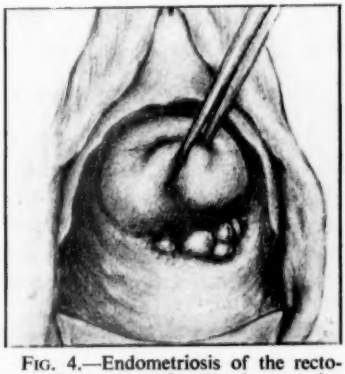

FIG. 4.—Endometriosis of the recto-vaginal septum, perforating the posterior vaginal fornix.

the rectal mucosa may occasionally be eroded, bleeding also may occur. On rectal examination the resemblance to a carcinoma may be very close but the proctoscope would reveal that the mucosa is unaffected and so clinch the diagnosis.

When the condition occurs in young women, and the symptoms are not severe enough to demand active intervention, it is obviously preferable to treat the condition palliatively and try the effect of male hormone. It would be very difficult to carry out local resection and in most cases, if the severity of the symptoms demands active measures, castration is the correct procedure irrespective of the age of the patient. Fortunately severe obstruction is very rare.

As regards the urinary tract, endometriosis is rare, but occasionally the ureter may be invaded by endometriosis of the ovary or pelvic peritoneum. Very rarely it may be primarily affected—Mr. Oswald Lloyd has recently had such a case in which two strictures were found in the ureter

together with ureteral endometriomatous polypi. Unexplained recurrent pyelitis may be caused by such a condition and an I.V.P. would reveal a hydronephrotic kidney. Treatment is resection of the affected portion and anastomosis or reimplantation into the bladder.

Endometriosis of the bladder is extremely rare. The symptoms are dysuria, frequency and hæmaturia, occurring at the menstrual periods and a tumour may occasionally be felt through the anterior fornix. Such cases may be confused with a carcinoma of the bladder, but the condition affects the muscle wall and not the lining epithelium and a biopsy would reveal its true nature.

Treatment is by partial cystectomy and reimplantation of the ureter into the bladder if required. If the patient is approaching the menopause castration may be attempted. Castration for endometriosis should be carried out by oophorectomy rather than by X-ray irradiation.

Treatment

Fibroids, if encountered in young women, should be removed by myomectomy. If menorrhagia is a symptom the cavity of the uterus should always be opened and explored. If *hysterectomy* is decided on, the total operation, with removal of the cervix, should always be undertaken, unless for technical reasons the operation may prove difficult or even dangerous.

Many *benign cysts of the ovary*, such as dermoids, chocolate cysts or simple serous cystomas, can and should be enucleated and the ovary conserved. Even when bilateral cystadenomata occur in young women it is usually possible to conserve some ovarian tissue near the hilum. When cystadenomata—serous or pseudomucinous—are found in women approaching the menopause the other ovary should always be removed.

If the tumour is macroscopically malignant, or suspected to be so, a total hysterectomy should also be performed.

If an abdomen be opened for a suspected acute appendicitis and an acute salpingitis be disclosed, the tubes should be left untouched and the abdomen closed. Even if a large acute pyosalpinx be present it is preferable not to remove it but to close the abdomen without drainage. With antibiotics and short-wave diathermy it is surprising how the majority of these cases resolve and occasionally leave a functioning tube.

[*May* 22, 1953]

A Film on the Murless head extractor in Cæsarean section was shown by Mr. J. H. Peel on behalf of Mr. B. C. Murless.

Specimens:

(1) **Brenner Tumour.**—Lieut.-Col. J. B. Neal.

(2–3) **Carcinoma of the Body of the Uterus Found During Investigations for Infertility.**—Dr. C. J. Champ.

(4) **Endometriosis of the Cervix.**—Dr. P. E. Hughesdon.

(5) **Ectopic Pregnancy with Tuberculous Salpingitis.**—Dr. G. W. Korn.

(6) **Adenocarcinoma Corporis Uteri Associated With a Blood-stream Metastasis in the Pelvic Colon.**—Dr. Peter Durham.

(7) **Miliary Tuberculosis Reactivated by Pregnancy.**—Dr. Norman Morris.

(8) **Squamous-cell Carcinoma of Bartholin's Gland.**—Dr. M. R. Fell.

(9) **Lymphosarcoma Involving the Generative Tract.**—Dr. M. D. Manion.

(10) **Anencephalic Fœtus Producing Obstructed Labour.** (11) **Fœtus Dicephalus.**—Mr. J. D. Andrew.

Section of Psychiatry

President—The Hon. W. S. MACLAY, O.B.E., M.D., F.R.C.P., D.T.M.&H., D.P.M.

[*February* 10, 1953]

On Ageing

By E. E. KRAPF, M.D., F.R.F.P.S.

Buenos Aires

THE process of ageing can be defined as a gradual transition from a condition of highly adaptable inadaptation—which is youth—to a state of increasingly inadaptable adaptation—which is old age. This formulation covers the ageing both of the physical organism and of the psyche of the individual: and those amongst us who consider the human being as an indivisible entity, will not find this surprising. Others, however, may feel that such definitions are nothing but a play on words. What—they might ask—has adaptation in the biological sense to do with adaptation as a psychological phenomenon? Is it not just one of those dangerous equivocations which, by a mere verbalistic trick, carries the problems of one series of facts into an entirely different sphere, and which, if accepted uncritically, is a well-known source of scientific error? One would have to show adaptability to be essentially the same thing in both realms before one could hope to convince these critics, and this is my intention in this paper. I believe that talking about "psychosomatic holism" and the like is rather meaningless if it cannot be demonstrated that one is dealing with truly "anthropological" (that is, biologically and psychologically equally significant) structures, and in this sense I take the anthropology of ageing to be a paradigmatic case of concrete psychosomatics.

I began by introducing the concept of adaptation. I must now clarify it and say that as a psychiatrist I am referring to the "adaptation of the individual's behaviour to the conditions of civilized life". Thus we are not only interested in the relationship between ageing and simply biological survival, but also, and more particularly, in the relationship between ageing and the undisturbed continuation of the life of intellect and sentiment, which is man's specific heritage.

It is true that the content of this heritage varies to a certain extent in different social and cultural settings. Basically, however, it is the influence of ageing on intelligence and character which engages the psychiatrist's attention when considering the problem of adaptation and adaptability.

Intelligence and character depend for their full functioning on the existence of a healthy brain; and this gives the problem a distinct *organismic* aspect. This is the field which has so far interested psychiatry most; in other words: psychiatrists have shown a bias for studying that material impoverishment of the personality which is most easily measured in terms of a decrease of intellectual performance.

My own earlier work in the psychopathology of old age—my publications on the psychiatry of arterial hypertension and on the presenile psychoses—deals predominantly with those brain aspects, and I feel that in this direction there is still an ample field for research. Especially interesting results can, I think, be expected from further progress in our knowledge of chemistry and the physico-chemistry of the ageing brain. I believe for instance, that a deeper understanding of the reactions of the central nervous system to nutritional hazards and biological stress in general will go a long way in explaining why different "functional divisions" (in Jackson's sense) react differently to the onslaught of the passing years. Such insight will probably bear out the clinical findings of what we might call the "brain topological" school of psychiatrists, the founder of which was the immortal Hughlings Jackson, and which counts amongst its prophets men like Wernicke and Kleist, Arnold Pick of Prague and Paul Schilder of Vienna and New York. We have, in fact, every reason to admit that Vogt's conception of topical vulnerability (pathoclisis) is particularly applicable where—as in senile disorder—there is in all likelihood an abiotrophic factor involved.

I have no doubt, however, that awareness of the vast possibilities of the organismic approach does not exclude the realization that we need also a somewhat *less material* type of research. Specialization in the encephalopathic aspect of ageing is bound to lead to a scotomization of those clinical features which cannot simply be considered as potentially measurable subtractions from a normal level of performance. This is, in my opinion, the main reason for the remarkable difference in attention paid by psychiatrists to disorders of intelligence on the one hand and of character on the other—although the character disorders are just as often determined by brain lesions as are the intellectual disorders.

In facing the problem of ageing from a psychological point of view, we must, of course, avoid being unilateral in the opposite sense. This approach tends to induce a characterologic bias (in other words: to make the worker overlook the measurable, viz. intellectual, decline of the ageing personality) in spite of the fact that intellectual shrinkage (or lack of development) can be just as psychologically determined (that is: motivated) as a change in character. All the same, it is, in my opinion, perfectly legitimate to use *the senile character* as a starting point for our present enquiry; that is to say, to look for the essential structures of personality ageing not in senile dementia, but rather in the behaviour which prevails in "ordinary" people of advancing age (and which, in

psychiatric textbooks, usually appears as those traits of "normal" senility from which, in almost imperceptible transition, the symptoms of senile dementia are said to develop).

Wilhelm von Humboldt wrote, at the age of 67, in a letter: "A serious, important and annoying point in old age is the uncertainty which accompanies at least me always, whether the years do not inadvertently cause a weakening of the spirit or of the character. . . . Everything wanes with time, and to this there has to be added that the soul depends on the body. One rightly distrusts one's own judgment, because its sharpness must have been affected by that very shrinking. Even worse is the lack of firmness in judgment. It is the irresolution of the character which extends itself from acting to thinking, since everything spiritual in man's intimacy is always in inseparable relation. But what worries me most is a sort of sleepiness of the soul, a state in which it runs around in a circle which it has known for a long time, imagining thus to live in satisfactory activity."

This analysis is an important document. Humboldt begins by stating his fear of intellectual decay—what he calls an affection of the sharpness and lack of firmness of the judgment. But what worries him even more, and quite rightly so, is the character disorder beyond and partly behind the "weakening of the spirit", that "irresolution which extends itself from acting to thinking" and that "sleepiness of the soul" which makes the old "imagine" that they are satisfactorily active, although, in fact, they do nothing but repeat the same patterns of behaviour over and over again. It is not difficult to find for these two features precise terms in modern parlance: what Humboldt describes is *lack of initiative* and *excessive habituation*, a twin pair of traits, which I consider basic for the better understanding of psychological ageing.

I spoke of a twin pair of traits, because lack of initiative and excessive habituation, are, in my opinion, completely interdependent. Every habit has once been an initiative which later had to turn into a habit in order to allow for new initiative. In our habits we let our past act with automaton-like determination in order to set our mind free to move on towards the future with elastic initiative. They are both, of course, equally necessary, but while in our habits our past history produces our acts, in our initiative our acts produce our future history.

"Juvenes enim", says Thomas Aquinas (drawing as usual from Aristotle), "multum habent de futuro et parum praeterito; et ideo, quia memoria est praeteriti, spes autem futuri, parum habent de memoria, sed multum vivunt in spe." Continuing our earlier train of thought, it does not take much to transpose this theme into the key of old age: "Old people have little future and much past: and therefore, as memory is the past's, but hope the future's, they have little hope, but live very much in memory." And this formulation leads us immediately to the conclusion that the lack of initiative and the excessive habituation which we considered fundamental for the psychological structure of old age, spring from an even more fundamental anomaly in the relation between the individual's past and future, or to put it more concretely; from an *atrophy of the individual's ability to project himself into the future*.

This "atrophy", responsible as it is for that tyranny of the habits, which makes ordinary old people psychologically so well adapted to routine and so little adaptable to new emotional and intellectual requirements, is nevertheless not only of significance in the realm of purely external behaviour. Its roots are deeply embedded in the life of the instincts. All instincts tend somehow towards the future, but none more than the sex instinct, the inhibition of which produces, almost automatically "neurotic" regressions into the past. On the other hand, it apparently transcends the sphere of more or less body-determined impulses and acts on and enters into the anthropological experience of time right up to the highest possible levels of the life of the spirit. "The most terrible thing about old age", said Ramon y Cajal, at the age of 69, "is not to have a tomorrow." But it is not the chronological "tomorrow" that he has in mind, it is the spiritual one; and it is only too easy to show to what extent for many old people "living in memory" means "having little hope" of the possibility of "fulfilling" themselves, and therefore experiencing a desperate "horror vacui" *vis-à-vis* the naked spiritual emptiness of their remaining years of biological existence.

As a typical example I mention that world-famous gallant, Casanova. At the age of 47 he complained in his Mémoires, "What a difference had I to face at comparing the state of my body and soul in that first youth with my life now. Now I found myself as unhappy as I had felt happy then; no more glittered before my eye the beautiful perspective of a happy future. . . . The twenty years which perhaps remained and on which I believed I could count only showed me a foggy perspective. . . . Everything seemed sad and desolate to me. . . . Everything made me aware that for me it was only a question of making as agreeable as possible an unavoidable decline, the invariable end of which is death." What a contrast between this black despondency and the supreme confidence of Goethe, who told Eckermann at the age of 80, "While it is day, we shall certainly keep our head high, and while we can still create, we shall not give in", an attitude of hopefulness which doubtless reflected to some extent his ability to take a physical interest in women even then, but which is, I think, even more closely related to his only slightly diminished ability to project himself spiritually into the future. It is well known that Goethe was capable of original literary creation almost to the time of his death, and the "product" as Charlotte Bühler so rightly says in her excellent book on "The Human Life Span as a Psychological Problem" "exercises . . . the function . . . of stimulating the individual and taking him beyond himself in his expansion".

I touch on this point just now in order to show the true anthropological nature of the disorder of the old which I called the atrophy of effective self-projection into the future, a demonstration which

I consider of fundamental importance for an understanding of its role as a genuine "*trouble générateur*" in E. Minkowski's sense, in other words: as a psychopathological structure which is *hierarchically and genetically prior* to the clinical syndromes and symptoms which we observe in ageing people. But I am quite aware that it is hardly sufficient without a corresponding deductive analysis of these syndromes and symptoms. Let us then see to what extent they can be understood as manifestations of the atrophy of the ability of self-projection into the future, and let us begin with the well-known trait of *senile avarice*.

Why are people stingy? Because they do not have enough? Hardly. In most cases miserliness springs from the (justified or unjustified) fear of not earning enough. He is stingy who brings a fortune from the past, but fears to be unable to "make" money in the future. It is not true that avarice causes anxiety, but it is true that anxiety causes avarice; and the anxiety which so often makes old people mean is only the despondency of people without hope in the future. There is no better case history of pathological stinginess than Molière's "L'Avare". Harpagon is an old man, and a man who suffers terribly from the horrible anxiety of the futureless.[1] He knows that he must live on what he brought from the past. If he loses it, he has no hope left, there is only death. And so, after he has lost his fortune he shouts rather like Casanova in his Mémoires, "It is impossible for me to live, it is finished, I cannot go on, I die, I am buried" (Act IV, Scene 7). The same sequence of events, in fact, which we observe often in certain patients: *anxiety*, *paranoid ideas* of being surrounded by thieves, and finally *depression*.

The problem of what the *experience of time* means *in vital depressions* has engaged the attention of some of the most acute thinkers in modern psychiatry, for example, L. Binswanger, E. Straus, von Gebsattel and others. Here I should like to quote E. Minkowski's version of the basic disorder: "The march of life is now transformed, the free march towards the future cedes to the impossibility of tackling the situations which life places before us, in the time span which we can dedicate to them without compromising the future, just as it cedes to the feeling of an unescapable determination by the past." Seen like this, vital depression can almost be called a precocious episode of old age. It cannot surprise us that a disorder which is (according to E. Straus) characterized by a lag of "ego time" with reference to "world time" should appear particularly often in persons who, like the ageing, suffer from having a time scheme which is more or less devoid of future, and who, therefore, are severely handicapped in maintaining a healthy rhythm in their "march of life".

Memory is considered to belong to the intellectual sphere of the mind. Freud has made this attribution rather debatable, and systematic modern studies—I mention only David Rapaport's monograph (1942)—prove its dependence on emotions to an astonishing degree. There is, however, no doubt in my mind that Hamilton is right in saying that several facts of clinical experience tend to support the supposition that the mnestic deficiencies of aged persons could be a partially psychogenic phenomenon. Many of the memory disorders of aged persons which are attributed to structural changes in the brain, can, in fact, be interpreted as a consequence of the atrophy of self-projection into the future.

It is a generally acknowledged fact that old people forget recent events more easily than long past ones. What is, however, not so well known, is that the typical memory performance of old people with structurally intact brains includes a *hypermnesia for the events of their earlier years*. The so-called "anecdotage" of the aged is not always due to a lack of judgment. In many cases it is only the consequence of the heightened power of remembrance of a person who, having little future, is living predominantly in the past. It is not by mere chance that the best memoirs are written not by people in the prime of their lives, but by the very old, who on the strength of their advanced age "multum habent de memoria".

This statement requires some qualification. Samuel Johnson once said to Boswell: "There must be a diseased mind where there is a failure of memory at seventy." I would not find fault with this dictum, if instead of mind he had said "brain" and instead of memory in general, "recollection". Even old people with organically sound brains may suffer from a serious impairment of their ability to register the daily happenings (the "Merkfähigheit" of German psychology). I believe, however, that this is generally only a consequence of a lack of interest, of a resigned pessimism. "Only that is incorporated into memory which is worth while registering", says Gruhle. Let us compare this with the testimony of two old men. First Goethe (in his "Zahme Xenien") at over seventy: "Youth forgets because of a division of interests, old age forgets because of a lack of interests." Secondly, Ramon y Cajal, in his "The World as Seen at Eighty", "What we should remember, old people and young, is that memory is fixed by three mordants . . . interest, emotion and persistent attention", and with reference to the lack of memory registration, "everything is a question of time, interest and passion. What is bad, is that not all old people have sufficient will and patience. . . . Some lack enthusiasm, and in others there is much despondency".

Clinical experience bears this out. In some of my cases I could actually produce selective modifications of impressibility: these patients could be induced to register or not to register almost according to plan. The operative formula is very simple: When their creative powers are stimulated, the ability to register increases immediately. In this field—as in many others—everything depends on arousing an interest in *legitimate self-projection*, in giving the aged individual a *productive personal future*.

[1] Nothing is more characteristic than his avid inquiries after Frosine has prophesied him a life of one hundred and twenty years: "Do you think so? . . . Do you know something about this sort of thing? . . . Can that be true?" (Act II, Scene 5).

This is in my opinion one of the most important rules for the therapy and prevention of a pathological ageing process. For, if we do not provide for *legitimate self-projection*, the ageing person has a strong tendency to fill the intolerable vacuum of the tomorrow with more or less *illegitimate forms*. Amongst the psychopathic reactions which appear for the first time in the advanced age, there are those which can not be related to structural changes in the brain, but which are perfectly understandable as expressions of "time anxiety", "self projection panic" or whatever name one cares to give the basic emotion. I quote out of my clinical material the case of a man, who at the age of 65, developed typical hysterical stupor states when he had to give up his normal occupation and live on the generosity of his son. The same man is now 79 years old and mentally as healthy as could be (certainly not demented). A happy result which mainly stems from his having regained a personal productive interest.

One field where this approach is particularly illuminating is the *sex pathology* of the aged. The acts of exhibitionism and pædophilia which are sometimes observed in old persons are not always demential phenomena. On the contrary, those unfortunate sex criminals are often perfectly lucid and sometimes even strikingly intelligent. It is a fact that regressive sex behaviour appears most frequently in old people of high personality standards. (Hamilton is certainly right in stressing frustration as a causative factor, but this in its turn is not only due to direct external restrictions, but even more to the over-exigent super-ego which simultaneously determines an over-development of sexual inhibition and critical thinking.) The dynamics of such intellectually unexplainable conduct become, however, quite understandable if one remembers that making use of one's sex drive, even on the lowest level, means regaining some sort of short-lived productive interest in the future.

There are, of course, individuals who manage to be self-projecting without any medical help. A sound religious attitude, for instance, with all its hopeful implications of a personal future beyond the limits of biological life, is often a very useful basis for healthy psychological ageing. It is also undeniable that the structure of an individual's *interpersonal relations* is of the greatest importance for the development of his ability for self-projection.

This explains, no doubt, why social and cultural conditions have so considerable an influence on the rhythm and quality of psychological ageing. Recent American statistics (Pollock, Malzberg) show, for instance, a truly alarming increase in the number of psychiatric old-age disorders, while, on the other hand, one hears of a particularly low incidence of these troubles in China (Dunham). My own observations on the Philippine Islands also show quite clearly that a civilization which offers the ageing a distinguished or even a reasonable social role, tends to produce old people of surprisingly good mental health. Old age pensions seem to be a very dangerous gift if they are given in a highly competitive society which only takes an interest in "delivering the goods" quickly, and, therefore, has so little use for the thoughtful slowness of experience that it pays its old people—of course under the disguise of the highest humanitarian considerations—to "stay out and keep out" of circulation. Even within the competitive civilization of what we generally call the more advanced nations, there are marked social and cultural differences in the psychological ageing of certain groups. As Charlotte Bühler (1933) has convincingly shown, old people who actually function as grandparents, aged peasants who go on caring for their hencoops or their beehives, intellectuals who continue to plan or write far beyond the biological climax of their lives, in short, all those who do not cease to be fertile, because they have not lost their productive interests, have a good chance of ageing well.[1]

This is doubtless one of the most important starting points for sensible geriopsychiatric action both in therapy and in prevention.

To mention a few practical experiments in this direction, there is the employment of old women in needy families, where they can act as foster grandmothers, a technique suggested by Fremont-Smith (1952), which I have seen in operation in Minneapolis and which apparently has also been used lately in Milan; the conversion of part of a home for old men into a primitive garden city, where everybody has the right to do what he wants with his small plot of ground (Squassini's "Villa Esperanza", "Borough of Hope" in Buenos Aires); and the creation of Old People's Hobby Societies and Experience Pools (particularly in the United States). But I feel that even more can be achieved by personal guidance. Not everybody has the spiritual power of, say, a Sherrington, who, after dedicating what is usually called "a whole life" to the study of reflexes, could then successfully enter the entirely new field of philosophy of nature (*vide*: "Man on his Nature"). Many, however, can discover something new in themselves if they are properly directed. and thus the psychiatric problem of the advanced age is not a question of new organizations, buildings, and asylums, but of a careful nursing of the interpersonal relationships of the ageing.

The possibilities of psychotherapy and psychological prevention in the field of geriopsychiatry are, of course, limited, but they are certainly much greater than is generally acknowledged: a patient does not cease to have psychological problems because his illness originates in direct brain participation (or even gross brain pathology). There are, however, limitations, and not the least

[1]To produce a child, plant a tree and write a book is, in fact, according to an old Spanish poet, the ideal plan for a happy future. See also the beautiful example which Minkowski (1951) quotes from his own father's life.

important of these arises from the circumstance that even the atrophy of self-projection into the future is sometimes clearly related to the condition of the brain.

I have said that the roots of this "trouble générateur" lie in the sphere of the instincts, and this means linking it to the functioning of the mesodiencephalic centres. Whatever the extracerebral causes of mental ageing—nutritional deficiencies, originating in endocrine changes, seem to be among the more important factors—there is no doubt that the ultimate cause is cerebral: often enough an affection of the vegetative "instinct centres" which determine the biologic rhythm of the individual.

I refer here particularly to the so-called *amnestic syndrome*. The loss of memory which gave it its name is, in my opinion, far less important than the "timeless" impotence of prospection that represents the atrophy of self-projection in the organismic sphere. A particularly illuminating observation of this type is given by Courbon (1927). A lady of 80, whose mind is " constituted by the paradoxical mixture of a formidable loss of memory and a disconcerting conservation of judgment", "responds, understands, acts through habit and not through immediate reflection" (viz. initiative). Need I say more to show that the anthropological structure of this patient's disorder fits to a nicety into my general conception of mental ageing? Minkowski (1933), commenting on Courbon's case, asks himself whether one should not say that "she does not use her memory any more, because she has no tasks for it". I consider this question very well put, but would add that the basic disorder is even more general: patients with an amnestic syndrome apparently have very few tasks for any sort of mental activity. They certainly live, as Courbon says of this case, "dans le général et dans le présent". A general decline of spontaneous interest in positive object relations, a universal weakening of the autonomous striving for contact with concrete reality, a passive dozing existence in an almost exclusively "actual" world—which is not entirely timeless, but certainly lacks the personal time reference within a historically structured life scheme called "temporalization" by van der Horst (1932)—these are the fundamental disorders in the so-called amnestic syndrome, and this total atrophy of the prospective personality can, in my opinion, only be understood in terms of a deep modification in the sphere of instincts.

I therefore agree with Gamper (1928) when he relates Korsakoff's syndrome (and the delirious states connected with it) with nutritional or toxic dysfunctions (and/or lack of function) due to cerebral lesions which affect the vegetative system, especially with respect to those physiological events that constitute, like sleeping and waking, the organic basis for the anthropological "timeliness" (Zeitligkeit) of the individual. The frequent confabulations of Korsakoff patients cannot simply be explained as mere "fill ups" of amnestic "lacunæ", but are psychopathologically and pathophysiologically just as "dreamlike" as the "oneroid" symptoms of the delirious. If this were not so, the experiment of Bettlheim and Hartmann (1924) (who used Korsakoff patients in order to prove the objective reality of dream symbolization in the psycho-analytical sense) could never have been carried out. The brain events which lead to senile Korsakoff syndromes evidently operate a shift of the vegetative make-up of the person which is anthropologically identical with that which affects every one of us when at night we withdraw into the completely instinct-governed primitivity and the eminently presentist temporality of sleep and dream.

I would like to add that the secondary nature of the memory disorder in Korsakoff patients has already been suggested by the experimental studies of Brodmann (1902 and 1904), Gregor and Römer (1907) and Gregor (1909). As to the importance of habit determination and lack of initiative in these cases, I should like to quote Korsakoff's own description of his psychosis as an "apathetic confusion". Among the many later authors who have indicated the same trait, I would mention Bürger-Prinz and Kaila (1930), with whom I do not agree in every respect, but who elucidate very well the fundamental significance of what they call a modification of "the whole of emotional and instinct structure" in the amnestic syndrome.

Finally, a disorder of instinctive driving power is, in my opinion, also responsible for the "Einstellungstörung" which Grünthal (1923) considers decisive for the psychopathology of the amnestic syndrome: the gist of this "disorder of the capacity for the adaptative gliding of attention" is, in fact, that the individual is quite unable to bring changing situations into their proper focus—a lack of mental elasticity which, at this level, is predominantly a matter of insufficient initiative (and, conversely, excessive habit determination). It is generally observable that any major disorder in instinctive driving power means that the individual's behaviour is secondarily dependent to a higher degree on learned (habitual) "formulæ".

The preservation of these formulæ presupposes a correspondingly high level of structural soundness of the neo-encephalon, particularly of the cortex. If, as a consequence of senile degeneration itself, or of some vascular accident, these higher structures are injured, the picture changes. Now the disorder of behaviour mostly affects that which is essentially human in man's personality, reason, thought and speech. In other words, we enter the field of "dissolution" in Jackson's sense, and in the wake of this "negative" demential decline we encounter all sorts of "positive" syndromes of reintegration released on the lower levels. Here, however, we are up against *gross senile decay*, the essence of which is plain inadaptation and not the "inadaptable adaptation" which we considered characteristic in the ageing process of individuals who were not subject to mutilating reductions of the brain substance.

In actual clinical practice it is not always possible to keep the defective features of a geriopsychiatric case completely apart from what we might call its developmental shrinking. Modern brain pathology, particularly the work of Goldstein and his associates, has shown to what extent the inadaptation

through elimination of higher (especially cortical) structures forces the individual to adapt very rigid patterns of specific behaviour in order to avoid chaotic situations and "catastrophe reactions". It can be very difficult indeed to differentiate between "defect rigidity" (with its accompanying specific Einstellungstörung) and the progressive decline of adaptability which is the result of an over-determination by the past through loss of prospection and anthropological presentism. Quite apart from the obvious fact that the two series of phenomena will often appear together, it has to be realized that, in view of the natural instability of external conditions, an absolute inadaptabilty is practically equivalent to inadaptation. Natural death itself could probably be understood as a phenomenon of ultimate inadaptation through a complete loss of adaptability.

Such considerations, however, should not blind us to the existence of important differences between senile decay on one side and ordinary pathological ageing on the other: differences, which are highly significant for the respective events and phenomena and, in my opinion, more important than the ones which separate the psychological and the organismic aspect of the latter.

I have already pointed out that the atrophy of self-projection has a psychological and a physiological basis, and that both express a change in the time structures underlying psychological and physiological life. I feel, however, that one can penetrate even deeper into the anthropological groundwork of existence: Nathan Shock (1945) and others say that ageing can be described as a gradual decline of the homeostatic capacities of the organism. Anthropologically speaking, the capacities to which these authors refer doubtless belong to the category of adaptive initiative; the habitual adaptation to routine losses of balance is not primarily endangered. In other words: we can interpret the process of ageing in terms of the conception of "stress", such as it emerges as a psychosomatic (that is, not merely physiological) reality; and this way of looking at things allows us not only to see the pathogenetic similarities of different phenomena in general ageing, but perhaps even makes it possible to find a common genetic denominator for such basic events of ageing, in the psychiatric sphere, as for instance the gradual decrease of colloidal vitality in the brain (the importance of which has lately been stressed by von Braunmühl) and that psychological devitalization which according to von Humboldt's classical description, leads to "a sort of sleepiness of the soul".

In this sense, the study of pathological ageing proves with particular neatness that, as Rapaport says in characterizing Schilder's approach, "the gap between neurological process and neurological disorder on one hand and fundamental psychological process and psychological disorder on the other does not seem as wide as it does to most investigators, nor as narrow as it seems to those who would derive mental disorder directly from gross physiological change or vice versa". It shows in fact, that this field of research is full of promise for those who, like Schilder, believe in the possibility of achieving an understanding of the total personality and its diseases by studying "the processes that occur in the 'gap': the neurological basis of psychological manifestations and the use of neurological mechanisms in psychological changes".

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Dr. Martin Roth: There are three points in Professor Krapf's address which seem to me to have a particularly important bearing upon some practical and theoretical problems of ageing and mental disorder in old age.

(1) *The Relationship Between Senile Dementia and "Normal Ageing"*

The classical descriptions of mental diseases in old age would appear to suggest that senile psychosis is merely a severe form of the all-prevalent pattern of "normal" ageing. It is not difficult to understand how such views arose when it is remembered that half a century ago a high proportion of the patients who entered mental hospitals after the age of 60 ended their lives there. Those fortunate enough to be cared for at home were left, when the disease from which they suffered had been allowed to run its full course, "weakened individuals" to use Bleuler's words. Depressive paranoid and confusional types of illness as well as the continuously progressive dementias were therefore held to be adequately covered by the clinical concept of senile psychosis. When arteriosclerotic psychosis was differentiated, it soon came to be regarded as a numerically less important and ætiologically overlapping entity. And as most people who begin to show in old age some degree of impairment of memory, or excessive caution, loquaciousness, rigidity or emotional cooling, die sooner or later, it seemed natural for the older writers such as Kraepelin and Bleuler to build up their picture of senile and arteriosclerotic psychosis by imperceptible stages from a composite and caricatured account of the ordinary old person. Such views gained support from the fact that the pathological changes found in the brain of senile psychotics are commonly present, though in less severe degree, in the brains of ordinary old people (Gellerstedt, 1933).

However, advances in preventive and therapeutic medicine have extended the span of healthy and active life in old age. As a result, differences in the course and pattern of outcome according to clinical picture, have become evident among the mental disorders of old age that were not apparent before. There would appear to be at least five distinct forms of mental illness, two of them probably not essentially different in ætiology from the functional disorders of earlier life (Roth, 1953). If we were to arrive at these varying pathological forms of mental ageing by extrapolation from the characteristics of the normal old person, we should have to find at least five different types of normal ageing in fairly pure culture as our starting point. I think it would be generally agreed that a search for them would hardly be worth the trouble involved. Moreover, as Professor Krapf has pointed out, if the differences between ordinary senescence and senile psychosis were merely quantitative, we would expect that the clinical picture of ageing should extend from ordinary senescence at one extreme to senile psychosis at the other by insensible gradations. But this is not the case. Senile psychosis presents clinically as a specific disease with a clearly defined course towards disintegration and death in a relatively short time. There is too much in it that is pathological, inexplicable in terms of ordinary experience and qualitatively different from the picture of normal ageing. Nor does one often see the varying intermediate stages between the two phenomena that would be expected on the hypothesis that ordinary senescence and senile psychosis are one and the same process.

This older view has, however, received impressive support from the recent work of Sjögren (1952) on the genetics of Alzheimer's disease. Sjögren found evidence to suggest that this condition may be determined by multifactorial inheritance. He has suggested that ordinary senescence, senile psychosis and Alzheimer's disease were "threshold phenomena" due to the same pathological changes when these develop to three different degrees of severity. The view he has put forward is particularly attractive in that it would be the sort of phenomenon one would expect from Medawar's important hypothesis about the biological derivation of ageing. Medawar (1946) has argued that in a hypothetically immortal population, genes with favourable effects would tend to spread more rapidly among the chronologically young whereas those with pathological effects would tend to accumulate in the chronologically old. When a decrease in fertility in chronological old age had developed in this way, genes with undesirable effects would tend to have their age of manifestation postponed beyond the period of reproductive life. Now, once confined to the infertile members of the species, the genes causing diseases would be entirely removed from the action of natural selection. The gene frequency would spread and the condition would tend to become common. This enables us to see how a change like the senile plaque, which is so common in ageing that one cannot help wondering whether it is of any significance when present to a mild degree, can yet be an essentially pathological phenomenon that has been modified and disseminated by the action of natural selection. If it were indeed responsible for the range of variation in normal ageing as suggested by Sjögren's hypothesis it might well be quantitatively graded like the genetic contribution to intelligence and the neurotic constitution. Its occasional manifestation in a severe form would then be no matter for surprise.

The implications of this hypothesis will probably be fully explored in coming years by Sjögren's school, to which psychiatry all over the world is already deeply indebted. But Alzheimer's disease is rare, and Sjögren's hypothesis, as he himself is careful to point out, is tentative. Much more evidence will be required before we are entitled to assume that the senile plaques and neurofibrillary changes are the cause of the normal decline of intelligence and adaptability with ageing. For these are not always present in old people and may even be absent when the clinical picture is indistinguishable from senile psychosis. On the other hand the changes may be found not only in normal old age (Gellerstedt, 1933) but in neurological disorders without mental deterioration such as amyotrophic lateral sclerosis and encephalitis (Jervis, 1945), as well as certain acute confusional psychoses in early life whose nosological status is not at all certain. We shall also need to know a great deal more about the genetic basis of differences in mental ageing before we can hope to understand the relationship between its normal and pathological variants.

Meanwhile we must base our views largely on clinical criteria and these indicate, as Professor Krapf stresses, a clear distinction between senile psychosis and normal ageing. Thus patients developing a depression in old age often seem apathetic, rigid in their habits and may complain of some impairment of memory. Yet two years after admission over 60% are discharged from hospital, whereas over 80% of the senile psychotics have died as compared with 20% of the depressives (Roth, 1953).

But it may be that we shall ultimately achieve in this field a unifying concept of ætiology within which the differences between the mentally senescent and senile can yet be given scope.

(2) *The Influence of Culture and the Pattern of Life Upon Senescence*

This is a problem of great importance for a civilization confronted with the prospect of a rapid rise in the proportion of old people. Professor Krapf points out that there is much to suggest that the extent to which people decline as they grow old is not wholly decided by organic changes which are inevitable. To some extent the picture in old age is determined by the type of life pursued. To the descriptions of Dunham and others of the mental virility of old people in China where the aged are treated with veneration, he adds his own impressions in the Philippines. Dr. Margaret Mead, during a visit to this country last year, described to me similar impressions about the aged in Bali. Now relatively few people live to be old in such countries, and we must, therefore, be on guard against drawing premature conclusions. But there is much to suggest that there may be a truth behind such impressions that is of far-reaching importance for us. Thus creative people so often continue to create when they survive to old age that one is compelled to wonder whether their energy and drive are not in part effects rather than causes of their continuing productivity. In this connexion, there comes to mind Cattell's interesting suggestion about the nature of the intellectual change that occurs during ageing (Cattell, 1943). He suggested that there were two types of adult intelligence, the "fluid" and the "crystalline", the former based upon ability to perceive new relations and the latter upon long-established habits in a particular field, which no longer require "insightful perception" for their successful operation. It is necessary to ask whether a life-long quest for new ideas might not be associated with less "crystallization". Conversely is it not possible that, when intelligence is compelled to operate within a narrow field, as is often the case in our rigidly specialized civilization, the natural decline in the ability to understand and adapt to new situations which is at the basis of fluid intelligence in Cattell's sense is assisted and hastened. Longitudinal studies of the evolution of intelligence at different social levels and in different occupations should ultimately give us answers to these important questions.

(3) *The Role of Emotional Factors in the Ageing Process*

Professor Krapf points out that we have been too prone to regard the intellectual changes as the central and basic feature of personality change in old age, whether in normal senescence or in senile psychosis. We have paid insufficient attention to the change in the capacity to hope, strive and to feel passionately. Yet even in organic syndromes of a specific kind like Korsakoff's psychosis, the lack of drive and the flattening of emotion were important factors consistently associated with and in some measure causing the defect. In the most malignant of all degenerative disorders of old age, senile psychosis, the patient seems to deteriorate not only in intellect but in all mental and vegetative functions, becoming towards the end inert, affectless, physically cold, shrunken and immobile. The cause of death is often difficult to state in terms of conventional categories of illness. Pathologists commonly put "myocardial degeneration" on the Death Certificate. But if cross-examined about this they will usually admit that this is often convenient rather than accurate. "Senility" as a cause of death is an excuse for ignorance that we can no longer afford to accept. Some time ago a famous German pathologist Grünthal (1927) was struck by the rapid vegetative involution of one of his patients some time before death. He looked for an explanation in the diencephalon and found it in the degeneration of grey matter in the neighbourhood of the third ventricle. It may be that the striking recent advances in our knowledge of the neuro-anatomy and neurophysiology of the diencephalon will bring in coming years some shift of interest from the cortex to subcortical structures in the neuropathology of ageing.

One final word about depression in old age. Many of the old accounts would lead us to believe that this is natural to the aged and Krapf's quotation from Cajal suggests that the great neuro-anatomist believed this to be so. Yet there is much to suggest that where this is sustained and consistent, the individual is suffering from a disease not essentially different from that in early age, and capable of responding equally well to treatment. There is often so much for the old person to be depressed about that in sympathy with his plight there is a tendency to interpret this as a disintegration under the stress of adversity or a perfectly normal or understandable reaction. In this way it is easy to overlook the indications for treatment that will in many cases produce sustained recovery. This is being realized to an increasing extent and we need not therefore feel despondent about depression in old age. It is the organic psychoses of old age that have so far largely defeated our efforts to alleviate them. Here further investigations into ætiology and treatment are urgently required. It will be evident from what has been already said that what we learn is likely to shed light not only on senile and arteriosclerotic dementia but also on some of the fundamental problems of ageing itself.

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DISCUSSION ON THE SURGERY OF TEMPORAL LOBE EPILEPSY

Dr. Denis Hill (Department of Clinical Neurophysiology, Institute of Psychiatry): *The Clinical Study and Selection of Patients*

During the last three years five reports have appeared from North America describing operations upon the temporal lobes of man for the ablation of epileptogenic foci and these reports have been encouraging both from the point of view of the control of epilepsy and for the amelioration of the associated personality disorder. Between 1939 and 1949 Penfield and Flanigin (1950) had performed 75 such operations on 68 cases and their early success led them to perform a further 30 in 1950. 51 cases have been followed up, some as long as ten years. They reported a 52·9% success; 27·4% of their cases having had no fits at all since operation, 25·4% one or two fits and then cessation, and a further 25·4% were improved. In only 21·5% was the operation regarded as a failure. These writers give little information about the mental states of their patients, but report that although half the temporal lobe or more was removed there was no evidence for alteration of behaviour, no particular memory loss and no persistent aphasia; nor was there any defect of initiative or capacity for decision.

Bailey and Gibbs (1951) reported on 28 patients. 14 had been committed to a mental hospital; all were serious social and economic liabilities. Following operation 6 were discharged from hospital and 7 became self-supporting. Major seizures were reduced in 15 cases and ceased altogether in 9. Psychomotor seizures, which had occurred in all 28, ceased in 17, were reduced in 8, and remained unchanged in 3. 16 of the patients were psychotic and 8 of these became quiet in behaviour, but only 2 became free from thought disorder. These writers considered that the mental status of their patients was remarkably better in 3, moderately improved in 15, unimproved in 8, and worse in 2. They claimed that the operation had a favourable influence on 64% of their patients. Green, Duisberg and McGrath (1951) followed 23 cases for periods up to thirty months after operation. 12 were free from seizures and in 9 there was a reduction in incidence. Only 3 were unimproved. In 8 of the 23 patients there was an improvement in the mental state. Smaller series have been reported by Morris (1950) and by Obrador (1953) from Spain. The total number of such patients reported in the literature is 132.

In these papers we are to report upon 14 epileptic subjects for whom temporal lobectomies have been performed by Mr. Murray Falconer at the Guy's-Maudsley Neurosurgical Unit. 2 of these patients have been referred by colleagues at Guy's Hospital and the remainder have been in-patients at the Maudsley Hospital. Dr. Desmond Pond has been responsible with me for the pre-operative clinical study of most of these patients and some of them have been under his care. Dr. G. Pampiglione has assisted us with the electroencephalography and has been responsible for the electrocorticography at operation which is now part of the routine procedure. My contribution is to discuss first the identification and selection of patients for whom this operation would appear to offer a hope of amelioration, and secondly to describe some of the results obtained. Mr. Murray Falconer will deal with the surgical aspects and, in the unfortunate absence of Professor Meyer, with some of the pathological findings which have proved most interesting and unexpected.

The necessary investigations which allow the surgeon to open the skull and resect a part of the brain with the confident expectation that he will remove the epileptogenic focus have been developed as the result of the new EEG techniques for the activation and identification of epileptogenic foci. At the same time, thanks to the work particularly of Penfield and Jasper at Montreal, that of the Gibbses, Earl Walker and others, as well as the more detailed clinical approach made to this subject by many workers, there has been a much greater understanding not only of the main sites of seizure onset in the brain but also of the probable pathways of spread from the focus. Remarkable advances in neurosurgery and anæsthesiology have allowed for greater control of the operative situation and enabled the neurophysiologist to join the surgeon at the operation and for them together to map out the abnormal excitable areas by electrocorticography. Thus the epileptogenic areas crudely identified from the scalp by the usual techniques of indirect electroencephalography can now be precisely located upon the surface of the exposed cortex or followed into the deep structures by means of depth electrodes.

The investigation of the type of patient with which we are dealing naturally falls therefore into the following stages.

(1) The presumptive evidence on clinical grounds that the epilepsy starts in the temporal lobe.

(2) The identification of the focus by electroencephalography and the demonstration of its constancy, as well as the relationship which may exist to structural changes in the brain revealed by pneumoencephalography or arteriography.

(3) An attempt to control the activity of the focus by anticonvulsants, failure of which leads on to the question of whether the total situation will be improved by surgical removal of the focus.

(4) The decision to proceed to operation when it is necessary to demonstrate by electrocorticography that the abnormal discharging area is confined to the anterior parts of a temporal lobe within that area which can be safely removed by surgery.

(5) Finally there is the post-operative treatment and rehabilitation of the patient which in cases of social deterioration is extremely important and may be very difficult.

The Pre-operative Study

Unfortunately the term "psychomotor epilepsy" has come to be used synonymously with temporal lobe epilepsy. The term "psychomotor epilepsy" was introduced by Gibbs *et al.* in 1937 when they made their first classification of the epilepsies based upon frequency and wave form of the EEG. At this time no attention was paid to the locational differences of such patterns. The so-called "square-topped wave" repeating at 4 per second which they observed to be frequently associated with behavioural automatisms was called the "psychomotor pattern". By 1948 it was shown by Gibbs *et al.* as well as by other workers (Jasper and Kershman, 1941; Hill, 1949) that the square-topped wave was not a wave at all, but a long duration spike repeating at 4 per second and that the commonest site for the focus for the discharge was a temporal lobe. However, such spike foci can occur from areas of cortex outside the temporal lobe and in some patients such foci can give rise to behavioural automatisms. The clinical evidence of automatism *alone* is not therefore certain evidence that the site of discharge is temporal. The evidence for this can, we think, be assumed with confidence only when the aura preceding the automatism indicates it. Many such patients with epileptogenic foci either in the temporal lobe or outside it have major seizures as well as behavioural automatisms. The important issue is not therefore the pathways by which the seizure spreads but the evidence showing from where it starts. This cannot be obtained by observing the patient's seizure although this may lateralize the focus to one side of the brain. The final evidence can only be obtained by asking the patient about his warning. As is well known the auras of the temporal cortex or deep temporal structures include a variety of visceral sensory, ideational and perceptual phenomena. Of these, epigastric, substernal and throat sensations are probably the commonest, and objective or subjective vertigo next. Olfactory, gustatory and auditory hallucinations are common and may be associated with *déjà vu* or unreality feeling. There may be an experience of echo of a word or thought or conversation previously experienced, or again a strong sense of being about to remember something but not doing so. The dream state involving visual or auditory hallucinations or both is not uncommon. In many cases intense fear is experienced and the patient may be aware of tachycardia and sweating. In our 14 cases 8 experienced epigastric sensations, 3 intense fear, 2 unreality feeling, 1 familiarity feeling, 3 olfactory or gustatory hallucinations; visual hallucinations with a dream state occurred in 1 and 1 patient experienced a compulsive idea.

Many workers (Gibbs *et al.*, 1948; Mulder and Daly, 1952) have recently emphasized the association between temporal lobe lesions with or without epilepsy and psychiatric disorder. Our own experience is entirely in agreement with this. Gibbs reported that 50% of such patients show severe personality disorder and in 25% of them psychoses occur at some time. Owing to the pre-selection of psychiatric cases at the Maudsley Hospital our figures for this are much higher and we find that there is a greater incidence of personality disorders in those patients in whom the focus is placed posteriorly in the temporal lobe rather than towards the temporal pole; a finding which is unfortunate from the point of view of surgery. Dr. D. W. Liddell, who has recently surveyed the epileptic in-patient population at Runwell Hospital has kindly allowed me to quote his findings which are to be published. A temporal lobe EEG focus was found in 50% of his epileptic patients which comprise 4·3% of the hospital population at Runwell. In 78% of those with temporal foci behavioural automatisms occurred. These figures are much higher than those given by Jasper for the general epileptic population, one in five of whom are believed to have a temporal lobe origin for their fits. There can be little doubt that temporal lobe epilepsy carries a serious risk of personality disorder and of psychosis. We have ourselves observed 13 cases of epilepsy with psychosis and in 11 of these demonstrated a temporal lobe origin for the seizures. In the 14 patients of this series 9 had automatisms and 11 major seizures. All but 2 had severe personality disorder showing excessive irritability and a liability to aggressive behaviour. 8 had been dangerously violent, 5 were paranoid, 7 had shown severe short-lived depressive episodes and 4 had fairly constant psychotic symptoms. The histories were characterized by multiple admissions to mental hospitals, casualty wards and prisons and attendance at public assistance offices. 4 of the 8 male adults had been unemployed for over a year prior to operation.

The EEG Investigation

In many patients the EEG is normal until the patient is put to sleep and basal electrodes used (Figs. 1, 2, 3). The focus may then be single or multiple, unilateral or bilateral, on the cortex of the convexity, buried in the sylvian fissure, or only seen beneath the anterior part from the sphenoidal electrode—in which case it may arise in the uncus or hippocampus. It is important to find the extent to which the activity spreads to the opposite side and whether another independent focus is to be found on that side. The best results of surgery are to be obtained, as Jasper *et al.* (1951) emphasize, in those with strictly unilateral, single foci. Whereas 12 out of 18 of their cases with definite unilateral foci had no recurrence of seizures at all, only 3 out of 14 had no recurrence when bilateral

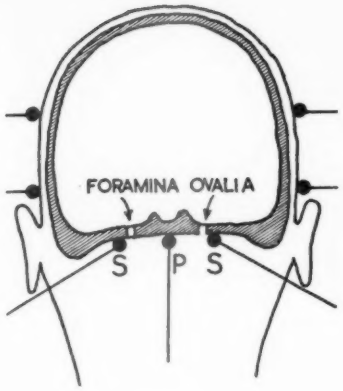

FIG. 1.—Sphenoidal electrodes. Schema of electrode arrangements using single pharyngeal (P) and bilateral sphenoidal (S) electrodes, the latter being connected in series with scalp electrodes on and above the temporal areas. The pharyngeal electrode is passed through an anæsthetized nasal passage and rests against the roof of the nasopharynx. Each sphenoidal electrode is inserted below the zygoma at a point 1 in. in front of the middle of the external auditory meatus, on a line drawn between the ala nasi and the incisura notch of the lobule of the ear. Passed upwards and inwards above the coronoid notch of the mandible the tip of the needle, which is the electrode, comes to lie just lateral to the foramen ovale.

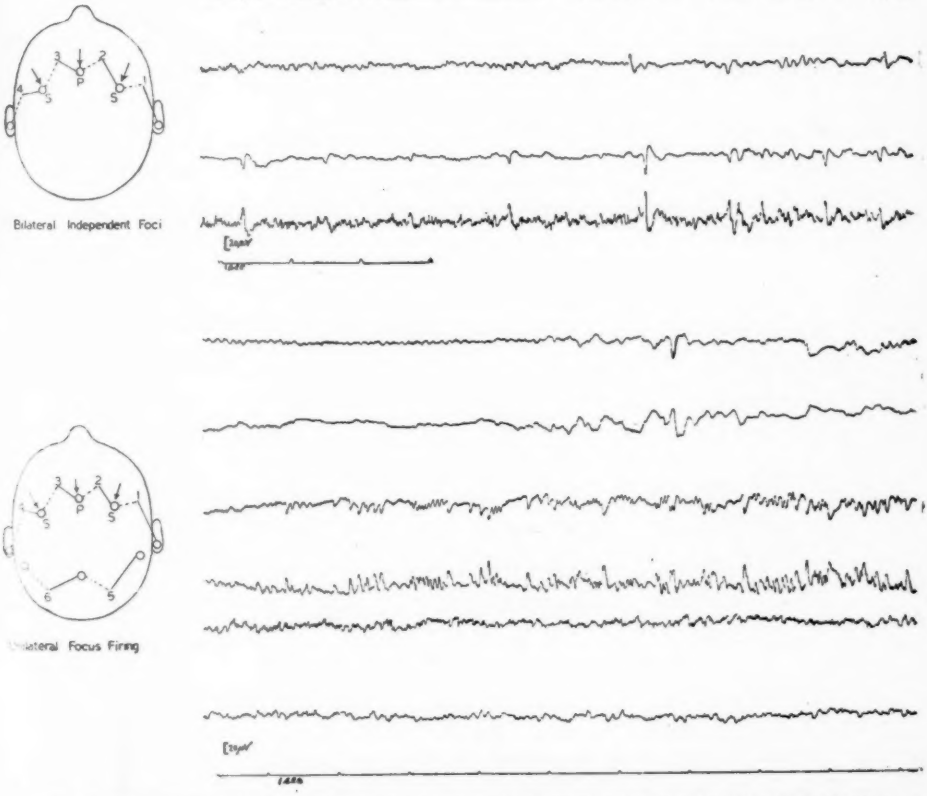

FIG. 2.—Shows two patients' EEGs. In the upper trace bilateral independently firing foci of spikes are seen at the two sphenoidal electrodes. The focus on the left side is the most active. In the lower trace a focus of spikes at the left sphenoidal electrode is firing very frequently. This initiates a slow wave disturbance on the right side at the right sphenoidal electrode. (S = sphenoidal electrode; P = pharyngeal electrode.)

or shifting foci were found. There is increasing evidence that in the course of time the unilateral focus is followed by another focus on the opposite side. I have observed this in a few cases studied over periods of years and Merlis (1953) recently reported that indeed, if studied long enough, 75% of cases become bilateral. The activation of foci at a distance and particularly on the cortex of the opposite hemisphere is frequently seen in cases of infantile hemiplegia with epilepsy, but it is gratifying that those who have followed cases of hemispherectomy where such foci have been found on the good side of the brain, find that they disappear after hemispherectomy. As Earl Walker once said, the epileptic focus is like a rotten apple in a basket of apples: leave it long enough and the other apples become rotten.

Our 14 patients were selected for operation upon the evidence, first clinical, then electroencephalographic, that a single dominant focus existed in the anterior part of a temporal lobe; secondly that the seizures had not been controlled by adequate anticonvulsant therapy. We were gratified when other evidence based on pneumoencephalographic or arteriographic studies pointed to structural change associated with the EEG focus, but were not discouraged by normal appearances. Some of these patients had been studied for years before operation. The 14 patients have had 82 separate EEG investigations made upon them spaced over intervals of weeks to years. Since operation 48 further EEG investigations have been made on the group to watch the effects on the epileptic activity. The first operation was performed two years ago, the last only a few weeks ago. Insufficient time to assess the lasting effects has therefore elapsed and the present study is in the nature of a report on the short-term results.

Results (Table I)

One patient, a woman of 41 with epilepsy since the age of 15, and a severe chronic paranoid hallucinatory psychosis, did not recover consciousness after operation and died after a few days. She was the first patient. Of the other 13, 10 have remained free from seizures, the follow-up period ranging from two years to a few weeks. However, 3 of these patients have experienced occasional premonitions of their fits. These 10 patients include all the patients of the series, 6 in all, in whom the EEG focus could be regarded as strictly unilateral, that is, showing no spread to the opposite temporal lobe. The 3 remaining patients have shown a reduction, in some degree, of their previous seizure frequency. These 3 patients had independent epileptogenic foci in the other temporal

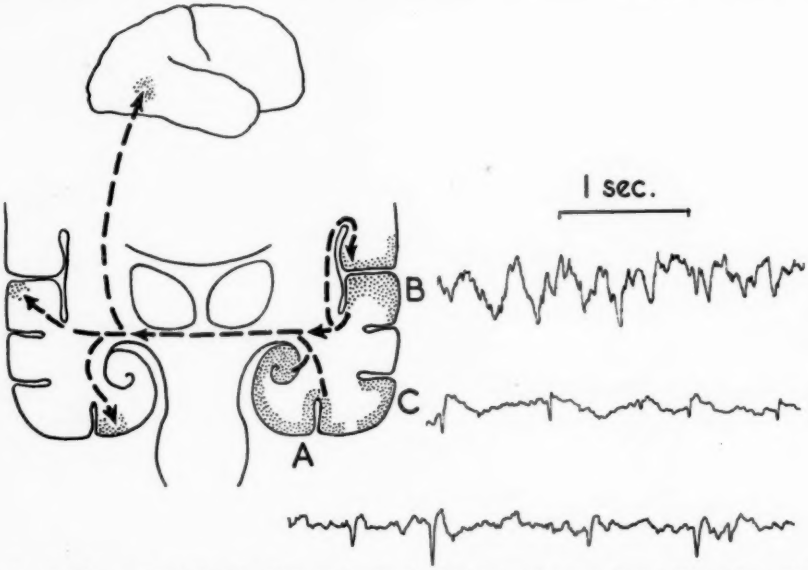

FIG. 3.—A schema illustrating the three main sites in the temporal cortex from which spike activity has been observed in patients with temporal lobe epilepsy; (A) from the anterior inferior surface at the sphenoid l electrode; (B) from the walls of the sylvian fissure and from the lateral surface of the superior temporal gyru ; (C) from the lateral surface and lower part of the temporal convexity. In (A) and (C) the spikes tend to be of short duration but when they are recorded from the scalp from buried cortex such as the sylvian fissure (B) the spikes tend to be of long duration, i.e. sharp waves. The diagram illustrates the possible effects of such foci in initiating secondary foci on the opposite hemisphere, either in the sylvian region, on the inferior surface or in the posterior temporal areas of the convexity.

lobe, which were observed pre-operatively, but regarded as secondary, or at least less active than the side upon which the operation was performed. A clear relationship between recovery from the seizures and improvement in the post-operative EEG state, has been observed. In the post-operative EEGs of the 10 patients who have been seizure-free, all were free from spikes or sharp waves except in 2. In a third a spike focus appeared on one occasion but disappeared later. On the other hand the 3 patients with recurrence of fits post-operatively showed EEGs with persistent firing of spikes, in 2 more frequently on the side contralateral to the lobectomy. We are therefore able to confirm the finding of previous workers that, at least as far as the short-term follow-up is concerned, the patients with strictly unilateral foci benefit most from surgery. In the others, the operation is followed either by a great increase in the epileptic activity in the remaining temporal lobe or by a reduction of such pre-existing activity. It would be important to be able to anticipate which of these courses is likely to ensue. It would appear that shifting or multiple contralateral foci and those which show a clear independence of that on the major side are of ill-omen, but more work on this is required.

TABLE I.—RESULTS OF LOBECTOMY IN 14 CASES OF TEMPORAL LOBE EPILEPSY

Case	Age	Onset ep. at age	Site of focus	Personality disorder	Post-operative		
					Fits	Personality	EEG
Ke	41	15	L	+++ (P)	Died		
S	5	1	L > R	+	F	I +	I ++
Pa	24	18	R > L	+++	I	I	NI
R	31	2	L	+++	F	I +	I
Ki	14	9	R	+++	F	I +++	I ++
Mac	45	2	R > L	+++ (P)	I	NI	I
F	45	18	R > L	+++ (P)	I++	NI	NI
W	22	12	R > L	+++	F	NI	I
V	23	21	L	—	F	—	I +
C	47	42	L > R	+	F	I ++	I +
Lew	43	35	L > R	++	F	I +	I ++
Le	38	5	L	++	F	I +	I ++
P	12	2	L + LF	+++	F	I +	NI
St	21	2	L	+++	F	?	?

F = fit-free. I = improved. NI = not improved. P = psychosis.
LF = left frontal lobe.

(Fits occurring in the post-operative period of four weeks have not been included in the results.)

Changes in Mental Status

These patients have been studied pre-operatively and after operation, not only by clinicians, occupational therapists and the nursing staff, but accounts from relatives have been taken by P.S.W.s and formal testing has been carried out by Miss S. Cox, Mr. V. W. Meyer and Mr. A. J. Yates of the Department of Psychology at the Institute of Psychiatry. There is general agreement among all observers that in the immediate post-operative period of hospitalization up to two months there is an improvement in personality in the form of greater warmth in interpersonal relationships, the patient being more co-operative and friendly. It is difficult to decide how much of this is due to the optimism and the relief of having passed through a major surgical procedure. No significant change was observed in formal intelligence and no change could be found in the Rorschach responses, except an improvement in verbalization which was noticeably more direct and simple in 4 patients. The greatest changes were in behaviour which were usually strikingly shown in personal contact with the tester and in the attitude to the tests. All but one of the 10 patients who have become fit-free have shown some degree of improvement in personality. A girl of 14 who had been deemed beyond control, broken out of remand homes, smashed windows in hospitals and could only be nursed in the refractory wards of a mental hospital, has returned to live with her parents where she has been now for nine months, to their great satisfaction. A man of 31, whose fits began at the age of 2, has since operation spent two months in prison for smashing a window in a public assistance office but thereafter was able to work for some months. He had been unemployed and unemployable for four years previously, but social deterioration is extreme and he is again on the verge of institutional care. He has not, however, suffered a fit since operation thirteen months ago. The best informants of the personality change are certainly the marital partners when these happen to be intelligent and one case, in which this was so, is worth quoting.

A married woman of 43 with temporal lobe automatisms in which she would undress herself, occurring every two to three days, either at home, in the street or wherever she happened to be, was paranoid, irritable, mildly hypochondriacal and coldly hostile to her husband and family. Interviewed some months after the operation since when she has been fit-free her husband said: "Although the results of this operation from a physical point of view are a miracle in that she has not had any seizures and her memory for current events is much better than it was and she speaks more fluently, yet from the temperamental point of view I think her condition is poor. Whereas before (operation) she had explosive periods, they were succeeded by periods of comparative calm and amiability, but now I am afraid her condition is evened out at a constant level of illenness, depression, quarrelsomeness and abusiveness. She abuses her son on the slightest thing."

Of the 3 patients whose mental status is regarded as not improved 2 had been regarded as chronic psychotic with paranoid ideas; both had bilateral foci, neither is fit-free since operation and both have shown a deterioration in mental state. Although the seizures have been fewer and milder in both cases, both have been readmitted to hospital because of aggressive impulsive behaviour and in one case certification appears inevitable. In one patient the increasing tension, depressive mood and irritable restless behaviour led us to think that he would be better if he had a recurrence of seizures. E.C.T. was administered and after 3 convulsions he showed great improvement and became calm and amenable, but only to relapse again a few weeks later despite a continuation of electroshock.

The third patient, a single man of 22 whose seizures started at the age of 12, was grossly alcoholic, aggressively psychopathic, abusive, insincere, homeless and unemployed. After his operation his seizures ceased despite bilateral foci, but his personality remained unchanged. He alone of the series showed an *increase* of libido, resembling the descriptions of Klüver's monkeys with bilateral temporal lobe ablations. In clear consciousness he began to expose himself and to masturbate in front of other patients and nursing staff, as frequently as twenty times a day. This behaviour was completely controlled by the administration of stilbœstrol and after a month this behaviour did not recur when the drug was withdrawn.

With the exception of the 3 patients who must be described as worse or at least unimproved by the operation, the procedure has been followed by an improvement in general health, seen in increase of weight and improvement of appetite. The effects on libido have been varied, most patients describing a reduction.

We must not ignore the fact that the majority of these patients have local structural lesions. However, the interesting fact is that the epileptic temporal cortex appears to have the effect, on occasion, of *fixing* or engramming the memory of previously traumatic events in such a way that when a seizure occurs these events may be relived with all their original affective intensity. Moreover the continued existence in the brain of such epileptic cortex would appear to exercise a disturbing influence not only on the patient's attitudes to the events which are engrammed but also in his total psychological adaptation. Following operation voluntary or induced recall of the traumatic experience is no longer disturbing and if all the epileptic tissue is removed, and probably only then, total psychological adaptation is improved: while of course it is only in a proportion that experiences engrammed and linked to epilepsy occur, our acquaintance with a larger population of temporal lobe epileptics suggests that the phenomenon is not at all uncommon. But it must be emphasized that personality deterioration occurs in patients in whom no engrammed experiences are demonstrable and therefore personality deterioration cannot be related directly to their existence. However, in many of these the epilepsy has started in infancy or childhood and it is now a common observation of ours that after years of temporal lobe epilepsy, not only do elements of the aura disappear but the patient cannot even recall the fact that on a previous occasion, perhaps years before, he has described them to his doctor. Since epilepsy of the temporal lobes appears to carry such serious risks for the personality, we cannot afford to neglect any evidence suggesting how the disturbed physiology may affect psychological functions. Penfield's remarkable studies in which he has shown that it is possible by electrical stimulation of the exposed epileptic temporal cortex to cause the conscious patient to relive previous experiences have aroused the greatest interest and enthusiasm. They will remain the model and the stimulus to all those who, like ourselves, hope to work in this interesting field.

One further issue, of some importance to the problems of epilepsy, must be mentioned. Many hold that the epileptic seizure is cathartic or to use a physiological term, homeostatic. Many have treated the psychotic epileptic, whose seizures have become infrequent, by E.C.T. and noted temporary improvement. The tension and irritability which may precede the fit in some patients is relieved by its advent. One of our 3 patients whose personalities showed deterioration after operation was treated with temporary benefit by E.C.T. Although reassured by the results of the American work I was concerned that these operations might not be followed by an increase in psychosis. This certainly occurred in one and possibly two patients who were psychotic pre-operatively, but both had active epileptic foci remaining and both had occasional seizures after operation. There has been no patient in whom the seizures have ceased, and the EEG firing areas ablated, whose personality has not benefited from the operation. The best results have indeed occurred when these two conditions have followed operation and a structural lesion been found in the excised tissue. This is in agreement with the observations of Green, Duisberg and McGrath (1951).

At the present time our limited experience would suggest the following tentative conclusions regarding the results of surgery in these 14 cases.

(1) Patients with seizures of temporal lobe onset in which the focus of onset is strictly unilateral can expect to benefit from the point of view of seizures, all 6 cases of this type being fit-free. Of 7 cases with evidence of firing in the contralateral temporal cortex, 4 became fit-free. With a longer follow-up this good result may have to be modified.

These results are in general agreement with those of previous workers.

(2) Improvement in personality occurred in some degree in all but 3 patients. 2 of these were

psychotic patients whose fits recurred after operation. The other was grossly psychopathic, alcoholic and homeless prior to operation. All 3 patients had bilateral EEG foci. The combination of bilateral EEG foci with psychosis or severe personality disorder would appear to be a contra-indication to surgery.

(3) The decision of whether any given patient is likely to benefit from temporal lobectomy, can only be made on EEG evidence demonstrating the constancy of the site of the focus, its location in a site available to surgical ablation and the absence of other foci in neighbouring parts of the cortex beyond the reach of surgery. Routine direct electroencephalography can only give approximate answers to these questions. Once the decision to proceed to operation has been made, it is obvious that direct electrocorticography can give the surgeon more precise answers to these questions, and will inevitably take its place, we believe, as an essential part of the procedure.

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Mr. Murray A. Falconer: *Surgical and Pathological Aspects.*

Epilepsy arising in the temporal lobe can result from a wide range of lesions. Some of these, such as neoplasms, vascular malformations, porencephaly and scars from penetrating injuries, can be readily recognized by neuroradiological studies, and lend themselves to surgical intervention with, usually, a favourable result. However, they account for only a minority of cases. Mostly in temporal lobe epilepsy the clinical and radiological investigations prove negative, and even the surface of the brain when exposed at operation shows little or no abnormality. It is with such obscure cases that we propose to deal.

Considering that electroencephalography will frequently disclose a focus of epileptic activity in the anterior part of one or both temporal lobes, it is not surprising that several neurosurgical centres have attempted to treat cases by operation, particularly when the focus is unilateral. Morris (1950), Bailey and Gibbs (1951), Green, Duisberg, and McGrath (1951), and Obrador (1953), for instance, have each recorded their experiences with a few cases. Various operative measures have been tried, including section of the white matter of the lobe (lobotomy), and ablation of the superficial temporal convolutions (gyrectomy), but so far the most encouraging results have followed upon removal of the temporal lobe itself (lobectomy). The extent of the lobectomies, however, has varied, in some instances being limited largely to the temporal pole, and in most instances the hippocampus and uncus have been left in situ. Consequently little opportunity has been afforded for studying the histological changes which affect these deeper parts of the temporal lobe, although in several cases atrophic changes have been noted naked eye.

Penfield and his associates (Penfield and Baldwin, 1952; Earle, Baldwin, and Penfield, 1953) have recorded the largest experience. In 100 out of 157 patients with temporal lobe epilepsy submitted to operation, Penfield observed macroscopically areas of sclerosis and atrophy, which usually affected the uncus, hippocampal gyrus, and the anterior part of the first temporal gyrus. These changes were ascribed to birth trauma, and it was postulated that they resulted from transient interference to the blood supply of the temporal lobe during parturition, when because of head moulding the uncinate regions were temporarily herniated through the tentorial opening. The remaining 57 cases were accounted for by post-natal injury, intracranial infection or neoplasm. These views relating to "incisional sclerosis" represent a distinct change in observation and interpretation from those of Penfield's earlier paper (Penfield and Flanigin, 1950). Penfield has yet to report in detail the symptomatology of his various patients, but it would seem that few of them had pronounced psychiatric features. He has also to indicate what are the results of surgery in his recent material. However, in an earlier paper (Penfield and Flanigin, 1950) he claimed a 52·9% success (i.e. cure) rate with a further 25·4% of patients appreciably improved. In his cases the uncus and hippocampus and other deeper parts of the temporal lobe were removed by suction, thus precluding their detailed histological study.

Personal Experiences

During the past two years, at the Guy's-Maudsley Neurosurgical Unit, we have operated on 14 patients with intractable temporal lobe epilepsy in whom careful clinical and neuroradiological

studies had been negative from the viewpoint of tumour, vascular malformation, or similar gross abnormality. Although we made the diagnosis of temporal lobe epilepsy from the clinical features, it was generally on the EEG evidence alone that we determined on which temporal lobe we would operate. Indeed, in 5 cases air encephalography disclosed a perfectly normal ventricular system, while in the remaining cases the temporal horn on the side of the EEG focus was either slightly larger or slightly smaller than on the presumed normal side. The most significant finding, however, was when one-half of the cranial cavity was slightly smaller than the other. The EEG focus was always on the smaller side.

Operative Technique

At first we did not have electrocorticography available to delineate the irritable area, and so at the outset we adopted the policy of removing as much of the affected temporal lobe as possible without crippling the patient. In this way we hoped not only to remove the epileptogenic area, but also to secure the affected tissue for histological study. In our first 3 patients we spared the uncus and hippocampus, not realizing that these structures could be removed without danger. However, as one of these patients (Case Pa in Dr. Hill's Table I) continued to have fits and also still showed a local EEG focus in the temporal lobe, we operated for a second time and removed these structures, with some benefit.

In some patients we performed the whole operation under general anæsthesia, but in 7 we commenced the procedure under local anæsthesia so that we could stimulate the exposed brain, and plot the lower part of the motor cortex so obtaining a useful landmark. In 6 patients we were faced with amputating the dominant temporal lobe, and by stimulating along the line of the proposed excision while the patient was reciting nursery rhymes we were able to show that there was no arrest of speech from these regions, and hence that no permanent speech disturbance would follow operation. In 2 patients we succeeded in provoking a seizure. In all patients, however, elevation of the temporal lobe from the skull base caused pain, and consequently the later stages were completed under intravenous Pentothal anæsthesia.

The steps of the operation practised in most of our cases are outlined in Figs. 1 to 4. Starting at the sylvian point the incision ran backwards through the upper part of the superior temporal convolution to the foot of the rolandic fissure, and then it curved downwards to reach the inferior border of the temporal lobe a little in front of Labbé's anastomotic vein (Fig. 1). Then the incision was steadily deepened to expose above and anteriorly the insula and the upper bank of the sylvian fissure still covered by the pial mantle of the temporal operculum, and posteriorly to open the hinder part of the temporal horn (Fig. 2). Next the white matter was divided between the lower boundary of the insula and the temporal horn, thus laying open the temporal horn with the hippocampus in its floor and the choroid plexus above this (Fig. 3). The removal of the lobe was then completed by continuing the incision across the hinder end of the hippocampus on to its medial border, as well as along the medial border of the uncus (Fig. 4). The actual sectioning of the cerebral substance was made with a fine metal sucker, and most of the hippocampus and uncus was subsequently found to be preserved on the amputated specimen. Finely controlled diathermy was used for hæmostasis. Our operative removals involved between 5 cm. and 9 cm. of the length of the temporal lobe, an extent similar to that of the removals described by Penfield and Baldwin (1952). Recently we have been controlling our excisions by electrocorticography.

Results

Surprisingly little disturbance results from such a large excision. Each patient except one (a 5 cm. removal) has developed an upper-quadrantic homonymous hemianopia, but without being aware of it. 8 patients had the left temporal lobe removed, and 1 of these showed some aphasic manifestations, which, however, disappeared. Several patients have shown a transient oculomotor imbalance suggesting a partial III nerve lesion, and one actually showed a fairly complete palsy which fortunately also disappeared. Psychological testing has shown no constant disturbance of intellectual functions.

The therapeutic results have been encouraging, apart from our first case which died after remaining in coma for eight days. The craniotomy had been reopened on the second day, but no clot formation had been found. At post-mortem the uncus, which had not been removed, was found to be prolapsed into the tentorial opening. Judging from a recent temporal lobectomy for tumour in which a similar prolapse of the uncus occurred, we could have saved this patient's life had we been aware of this complication, by reopening the craniotomy and dividing the tentorium.

The remaining 13 patients have now been followed up for periods ranging from one month to two years. Two main generalizations can be made:

(1) Operation usually will either stop or diminish the epileptic attacks. In possibly 10 patients the attacks have ceased, and in the remaining 3 their frequency has lessened considerably. All 3 had bilateral foci although pre-operatively the focus in the operative side appeared to be dominant.

(2) The personality often shares in this improvement, but not always. In some of our patients a striking improvement occurred, but in at least 2 it was worse.

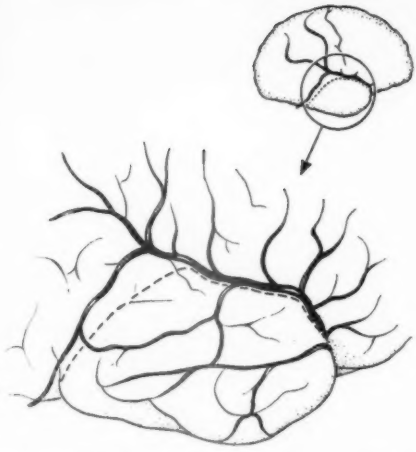

FIG. 1.—First stage of temporal lobectomy: The line of the incision in relation to the sylvian vessels and to Labbé's vein.

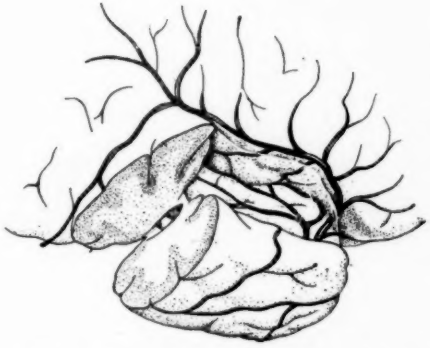

FIG. 2.—Second stage: The insula has been uncovered and the temporal horn opened.

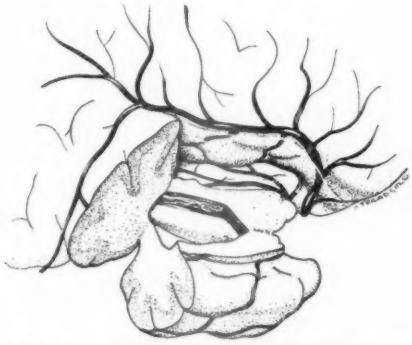

FIG. 3.—Third stage: The temporal horn has been opened exposing the hippocampus in its floor with the choroid plexus lying above it.

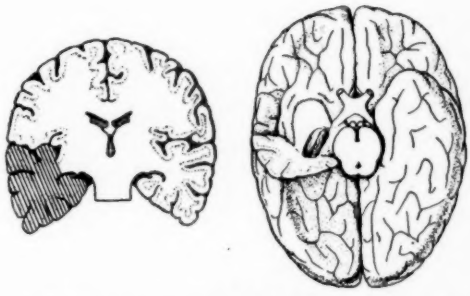

FIG. 4.—Representation of extent of temporal lobe removal at completion of operation. Note in the basal view that the roof of the third ventricle still remains as well as the choroid plexus.

Pathological Changes

Professor Alfred Meyer (who unfortunately is absent) has been studying the resected temporal lobes. In several cases we have observed sclerosis of Ammon's horn. The frequent presence of such sclerosis in cases of chronic epilepsy which come to autopsy is an old observation, and Professor Meyer several years ago reported on it (Meyer, 1939). The classical view has been that such sclerosis is the result of vasomotor and ischæmic changes which occur during the cyanotic stages of major seizures. In support of this view that such changes are secondary to the epileptic seizures and are not the cause of them, can be marshalled evidence that the cells of Ammon's horn are particularly vulnerable to a wide range of toxic processes. However, the long acceptance of this view should not blind us to the possibility of interpretations such as Penfield's, that sclerosis in this region may be primary to the epilepsy. Professor Meyer tells me that the brains of many chronic epileptics do not show these changes, even after a long history of severe attacks of *grand mal*. Ammon's horn sclerosis, therefore, is not an invariable sequel of cyanotic seizures.

Professor Meyer has also observed gliotic and sclerotic changes in other parts of the temporal lobe, and has been collecting a series of control sections from healthy temporal lobes for comparison. This comparison will require much time, and he does not yet feel justified in giving a pronouncement.

However, we as surgeons gaining experience of the consistency of various temporal lobes at operation have noted in several cases sclerotic changes as evidenced by undue toughness and yellowish discoloration of the white matter which have the distribution in the superior temporal convolution, uncus, and hippocampal gyrus described by Penfield. If Penfield's view is correct, then these changes precede the epilepsy and are the cause of it.

Other lesions found include two instances of a focal collection of astrocytes, oligodendrocytes, calcospherites, and capillaries, which might be termed a hamartoma or congenital abnormality (Falconer and Pond, 1953); a small meningo-cortical cicatrix involving the temporal pole; and a case of localized chronic leptomeningitis. In fact in each of our first 8 cases, in which pathological studies have been completed, some histological abnormality has been found in the resected temporal lobe, although the significance of these changes (particularly those concerning Ammon's horn) may be open to question.

Further Comments

These communications are merely preliminary, for we are still in the early stages of our experience, and cannot do more than generalize widely. The fact that we are encountering definite pathological changes in a surprisingly high proportion of cases and that subsequently our patients are being benefited as regards their fits, indicates that the type of epilepsy we are dealing with can no longer be regarded as idiopathic. It is really focal epilepsy anatomically determined because of pathological changes which happen to involve the temporal lobe. There is, moreover, no reason why the histological changes could not affect both temporal lobes, thus giving rise to bilateral independent epileptic foci. We have, however, not yet performed a bilateral temporal lobectomy.

So far we have operated on cases which have been crippled by the epilepsy, and which have in most instances been also crippled by a superimposed personality change. If, as we think, our operative intervention carries little risk to life or limb, then we are probably justified in accepting for operation cases with milder seizures and disturbances and without personality changes, but whose lot could be improved none the less. In the long run it may prove wiser to operate early and prevent the personality change, rather than to wait until the symptoms become flagrant.

Temporal lobe epilepsy is common, and causes much disablement in any community. Its frequency has been placed at between a fifth (Lennox, 1951) and a third (Bailey and Gibbs, 1951) of all epilepsy. The exact incidence of all epilepsy is not known, but an approximate figure is possibly 0·5%. Translated into terms of the population of the United Kingdom this means a quarter of a million epileptics and at least 50,000 sufferers from temporal lobe seizures. Many of these may be only slightly disabled, but any approach which promises to improve our knowledge of the subject and to increase our therapeutic effectiveness merits serious consideration.

I wish to thank Miss Sylvia Treadgold of the Department of Medical Illustration, Guy's Hospital, for the illustrations.

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Dr. G. Pampiglione: *Electrocorticographic Approach*

The detection of the abnormalities of cerebral function considered to be related to the initiation and spread of an epileptic seizure is the aim of a combined effort of the clinician, the surgeon and the electrophysiologist. At present applied electrophysiology is an expanding subject with many unknown aspects. The information given by this method of investigation may be, however, of decisive value in the localization of an area of abnormal function in the brain. Dr. Denis Hill and Mr. Murray Falconer have summarized the work done on this series of 14 epileptics with mental disturbances and seizures related to functional abnormalities in the temporal lobe. I shall briefly mention the studies done during operation (electrocorticography).

Electroencephalography, or recording from without the skull, gives a good deal of information about some abnormalities of cerebral function and may indicate the lobe mostly involved. Electrocorticography, or recording in direct contact with the surface of the brain, gives much more detailed information about small areas within a convolution or a sulcus which may be involved in the epileptogenic process. The relevant abnormalities are often recorded from areas appearing quite normal to the eyes of an experienced neurosurgeon.

In man, the pioneering work of Foerster, Grey Walter, Schwartz, Scarff, Jasper, Walker and their collaborators, has given us a good deal of valuable information both about the technical difficulties and the interpretation of electrocorticography. In the future with increasing knowledge, electrocorticography will help the surgeon to assess more precisely the extent of the area of abnormal function, and will help the patient by restricting the removal of healthy brain.

In this series of cases the programme was to excise the anterior part of the temporal lobe irrespective of the corticographic findings. This approach, justifiable in the present state of limited knowledge, will result in the accumulation of a good deal of data. This will give a lead in assessing some of the reasons for success and failure of surgical treatment in individual cases after they have been followed up for several years. As an example of the problems we are dealing with I shall describe 2 of the 4 cases studied by electrocorticography in the present series.

A boy of 12, under the care of Dr. D. A. Pond, had a complex clinical and social history. He was admitted because of frequent fits and outbursts of uncontrollable behaviour in spite of medication. Multiple pre-operative EEGs showed an area with abnormal electrical discharges in his left temporal region. At operation no macroscopic lesions were seen in the temporal cortex but the lobe was small. Electrocorticography showed abnormal discharges over most of the convexity of the temporal lobe, particularly in its anterior half, and from the pole and from the hippocampal convolution. In addition, frequent discharges were recorded from an area of the frontal lobe in a region about 1 cm. above the sylvian point. Intravenous Pentothal increased the amount of abnormal discharges as well as the complexity of the picture and also appeared to synchronize the firing of all areas. No clinical changes were noticed apart from the patient going to sleep. The white matter of the excised temporal lobe appeared rather hard and was brownish in colour towards the pole. Recordings taken from the inferior frontal area following the excision revealed that some electrocorticographic abnormalities still remained. Post-operative scalp recordings showed that the inferior frontal region remained abnormally active several weeks after operation, though the abnormality was not so severe as before operation. This boy is fit-free on medication. (Case P in Dr. Hill's Table I.)

A girl of 21, a patient of Dr. Denis Hill, with a marked educational handicap had rather complex seizures. Her EEGs showed a clear spike focus in her left mid-temporal region. This focus appeared constant without much spread both in the scalp and "sphenoidal" recordings during sleep or the waking state. Corticography, however, showed multiple and apparently independent firing areas maximal over the II and III temporal convolution. There was little abnormality at the temporal pole or towards the hippocampal convolution. Several focal spikes and some slow waves were seen from an area behind Labbé's vein and also from an area in the central region about 1 cm. above the sylvian vessels. Intravenous Pentothal in her case depressed and abolished these cortical discharges. In the immediate post-operative period there has been only one fit on the pre-operative medication, but the patient has experienced her old abdominal aura on a few occasions. (Case St in Dr. Hill's Table I.)

These 2 cases, though rather dissimilar, are of great interest and present to my mind similar problems. In the boy abnormal electrical discharges remain in the inferior frontal region and can be picked up by scalp recording. In the girl the remaining abnormal activity is in the posterior temporal and in the inferior central region, but recent scalp recording suggests that this is diminishing. In the boy Pentothal increased the abnormal firing and in the girl Pentothal diminished it. Both patients are at present free from fits.

These cases illustrate the difficulty in correlating clinical and electrical studies from the scalp, and the electrocorticographic findings. Will the electrical abnormality persist in these cases or will it subside? Will the seizures reappear in one, in both, or in neither of these patients? Or will the attacks be modified? These are the problems we shall be able to solve only in a few years' time after careful clinical and EEG follow-up. Perhaps then new problems will arise: will the patients' mental or personality disorders be changed and if so whether in relationship to or independently of the course of their attacks?

In addition the removal of a relatively large mass of brain—for instance, over one-half of a temporal lobe that includes at least some of the epileptogenic areas—may influence other potentially epileptogenic foci either way: it may make them independently active or may help in their disappearance, with or without the possible influence of medication.

From this small group of cases and from a few other cases not included in this series I have learned how difficult it is to compare one's own findings with other workers' experience in a relatively new field. This seems particularly relevant in the present series of temporal lobectomy cases which is from the clinical, electrical and pathological aspects far more complex than was at first thought.

I am indebted to Messrs. R. Cooper, P. St. J. Loe, and J. Theobald for their technical collaboration. To Dr. J. A. V. Bates and Dr. W. Grey Walter for their kind advice.

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Dr. D. W. Liddell: Temporal lobe epilepsy accounts for 50% of all epilepsies of varied æticlogy at Runwell, and in 78% of these cases behavioural automatism occurred.

The total incidence of epilepsy in mental hospitals seems to have varied little in the past seventy-five years, in spite of great advances in treatment. For in 1875 Jackson quoted the figures of Bucknill and Tuke, who estimated that 6% of patients in the asylums of that time were there owing to epilepsy. In a recent review of 1,100 patients at Runwell (Liddell, 1953) I found that epilepsy was the cause for admission in 47 patients—25 male and 22 female—or 4·3% of the total number. The probable reason for this is that temporal lobe epilepsy is poorly controlled by anti-epileptic drugs.

In the present series automatism was commoner among the male patients—13 males (52%) of the total male epileptics had automatism as opposed to 5 females (23%) of the total female epileptics.

The aura is of interest, for with the advent of automatism it appears to cease in a number of cases. This is only partially true, for if an attack is witnessed, the patient, immediately after an attack, will describe an aura, but a few hours later will completely forget it; then will, if reminded of it, rather shamefacedly agree that he can recollect such a feeling or idea. In this way a description of different auras may be obtained after various attacks. Normally the aura is thought to be constant for most patients. This is the rule when it precedes major fits.

In a certain number of cases of automatism the aura may last for some time, up to a minute or more, and enable the patient to warn those near him that an attack is pending. In such cases the aura is always remembered. It would thus seem that a minimum time of exposure is essential for recollection, for the longer an aura is experienced prior to an attack, the more likely is it that it will subsequently be remembered.

Not infrequently the aura or dreamy state occurs at times quite independently of any subsequent fit. This may well not be linked by the patient to his epilepsy.

A male patient, aged 38, following head injury developed epilepsy, preceded by an aura of unreality. After a year or so automatism developed following a transitory fit in place of the major epilepsy. About this time, when alone or reading, he became assailed by the thought that "I have robbed my father's safe" and this belief or thought lingered for a short while and it was associated with a feeling of great distress. It was in no way connected by him with his fits, but his wife had observed that he sometimes cried this aloud before his turn. She had investigated this incident with negative results.

Here a false memory forms the content of the dreamy state. The vocalization of a thought or feeling has been observed in a number of cases before a fit but does not happen if the dreamy state only occurs. It appears that when the discharge spreads sufficiently to cause a fit, vocalization might happen, but there is afterwards complete amnesia for this. Of interest is the fact that stimulation of this limbic area in animals causes vocalization.

Maclean (1952) and Maclean and Delgado (1953) have experimentally investigated the functions of the limbic formation in animals. They have shown that it is intimately concerned with behaviour, related to feeding in all its forms. In humans temporal epilepsy occurs most frequently at the meal table and the prodromata, often of a day or more duration, assume the form of aggression or hostility, noted by the nurses to be related to food.

Lastly, automatism may occur after major epilepsy, adversive fits, or after a transitory minor turn of such short duration that it may well be missed. This latter onset may be associated with the classical jaw champing. The frequency of the preceding fit is minor, adversive and major. The more severe the preceding fit the more violent and purposeless is the subsequent automatic behaviour, so that following the major fit the full-blown epileptic furor reaching homicidal intensity may occur. Following the minor fit, the behaviour approaches that of normal and on superficial observation may be missed by those around him, and is only noticed afterwards by the sufferer by some odd thing that he has done, such as adding up a column of figures and putting something very unusual as the total.

These patients, whatever their individual outlook on life, depending, of course, on their various personality traits, have in common a restless aggressiveness. They never fully settle to any task, often wanting to start something new before they have completed the job on hand. They work hard but fitfully, are quick to take offence over trivial incidents, and at times are openly hostile for no adequate reason. Following lobectomy they become friendly, concentrate on the job in hand and are able to sit and enjoy life. As one patient remarks "I feel satisfied and content now".

It is tempting to make a visceral comparison. Before operation they are hungry, restless, asocial, and have their fits, and afterwards they are replete, friendly, and cease to be explosive. In fact, they are changed from carnivora into herbivora.

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Section of Physical Medicine

President—DONALD WILSON, M.B., M.R.C.P.

[*October* 8, 1952]

A Study of Spinal Osteoporosis

PRESIDENT'S ADDRESS

By DONALD WILSON, M.B., M.R.C.P.

I SHALL discuss the diagnosis and treatment of spinal osteoporosis as it appears to a clinician. The investigation is incomplete because a correct analysis of the diet could not be carried out and the biochemical analysis of endocrine excretion was not attempted. In the complete investigation of this condition a metabolic ward, where food analysis can be done and the staff are trained to collect all the specimens required, is essential for scientific purposes. As this was not possible I shall present my paper as a study and not as an investigation.

The diagnosis of osteoporosis is a radiological one. The patient complains of pain or stiffness of the back, sometimes both, and on examination there is usually little to be found except occasionally kyphosis and localized tenderness. The radiologist in his report usually refers to the decalcification which is present and from that point the investigations commence.

The character of the investigation depends in the first place upon the concept of osteoporosis. Under normal conditions adult bone is subjected continuously to two processes, formation and resorption. Albright defines osteoporosis as the condition in which the osteoblasts lay down too little bone matrix, but the matrix that is deposited is completely ossified, thus differentiating the condition from osteomalacia where the bone matrix laid down is not fully calcified. Bone formation is due to the depositions of calcium and phosphate in a proteinic matrix which is laid down by osteoblasts. If the osteoblasts are inactive then insufficient matrix will be deposited and the alkaline phosphatase will be within normal limits; this is the usual finding in osteoporosis. If, however, the osteoblasts are active and lay down sufficient matrix but, owing to the ineffective absorption of calcium, this matrix is not calcified then osteomalacia appears and the level of the alkaline phosphatase is found to be high.

Of 36 cases of bone atrophy that were selected from the numbers investigated during the past twelve months, 15 had either a high alkaline phosphatase level in the blood, a history of injury or associated disease, or a benign tumour of bone. 21 cases had no such history and the blood chemistry showed no deviation from normal. The 15 cases were selected from a number seen during the past twelve months in order to compare them with the 21 cases which were unselected and seen during the period July 1 to November 30, 1951. The investigations of the 2 groups of cases were similar, namely:

(1) *History of past illnesses, particular stress being placed upon:* (*a*) Operations. (*b*) Gastro-intestinal disorders. (*c*) Diet.

To assess the quality and quantity of the diet was difficult and could only be judged very crudely. The patient was either asked to write out the food eaten on certain days or this information was obtained verbally. Finally the decision on the quality of diet was taken on the amount of first-class protein, milk and cheese, that they were judged to have taken.

(2) *Blood tests:* (*a*) Complete blood count. (*b*) Hæmoglobin. (*c*) Plasma proteins. (*d*) Sedimentation rate. (*e*) Calcium. (*f*) Alkaline phosphatases.

Of the 15 cases showing bone atrophy 8 had a high alkaline phosphatase (Table I), 2 had

TABLE I.—HIGH ALKALINE PHOSPHATASES

Age	Sex	Alkaline phosphatase	E.S.R. (Wintrobe)	Alb.	G.	Bence-Jones protein
42	M	72	60	4·0	10	+
46	M	40	48	4·1	7·2	+
56	F	64	48	4·4	4	+
48	M	50	60	3·6	4·8	+
55	F	35	49	4·1	2	—
74	M	22	62	3·6	1·6	—
64	M	102	37	4·0	1·5	—
68	M	36	24	4·2	1·9	—

metastases and 2 cases had Paget's disease. In 4 cases where the high alkaline phosphatase was combined with a high sedimentation rate, a reversal of the normal albumin-globulin ratio and the characteristic Bence-Jones protein indicative of myelomatosis were found.

FIG. 1.

Fig. 1.—An elderly man, has been taking stilbœstrol for a year; his sedimentation rate and alkaline phosphatase are now within normal limits, but this X-ray taken one year ago shows decalcification of the vertebræ with partial collapse of several and widening of the intervertebral spaces with herniation of the discs through the vertebral plates. He had been diagnosed as spinal metastases due to carcinoma of the prostate.

Figs. 2 and 3.—Man with multiple myelomatosis. His history is typical of the 4 cases of this disease that I found. There was a short history of pain and stiffness of the back and recent loss of weight. Clinical examination revealed nothing more but X-ray of the spine showed a general decalcification; no evidence of spinal collapse was found at this stage but the diagnosis of multiple myelomatosis was suspected by the high E.S.R. with a reversed albumin-globulin ratio. This was confirmed by the presence of Bence-Jones protein in the urine and typical myelomatous deposits in the skull.

The presence of these 4 cases of myelomatosis in the series indicates the importance of doing the Bence-Jones protein test in all cases of decalcification. It is a simple test which can be performed rapidly and cheaply.

Of the remaining cases of this first group of 15, 2 showed widespread decalcification due to associated disorders.

One is a case of presumed renal dystrophy in a man of 19. There is little to support this presumption beyond the statement that he is supposed to have had renal rickets between the ages of 8 and 14. He had had several greenstick fractures between 12 and 17, but when X-rayed recently, no evidence of pseudo-fractures could be seen. We could find no evidence of renal

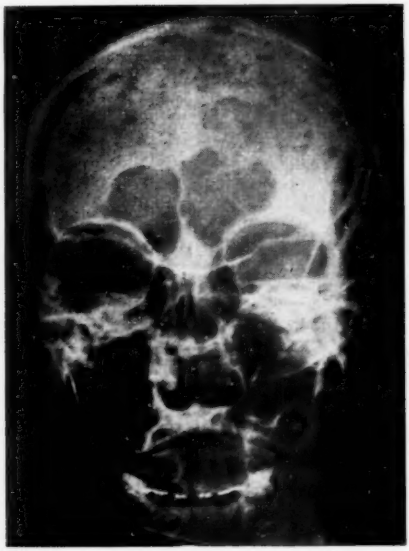

FIG. 2.

FIG. 3.

calculi and his urinary tests were normal. The calcium level was 10·5 and inorganic phosphorus 3·1 mg.%. As this man is performing his work satisfactorily he is reluctant to take time off in order to have this disorder investigated further. I have regarded him as having decalcification of unknown origin. In spite of the absence of Looser's bands, probably a diagnosis of Milkman's syndrome will be made.

FIG. 4.

Decalcification occurs in ankylosing spondylitis.—A case was under investigation for abdominal pain and the spondylitis was unsuspected by the surgeon but confirmed by the radiological examination of the sacro-iliac joints. The remnants of the barium meal that was taken to exclude a peptic ulcer can be seen but at the same time the typical "square" profile of a vertebra in ankylosing spondylitis and the decalcification of all the vertebræ is visible (Fig. 4). This patient had been receiving a satisfactory diet.

Table II shows the great predominance of females, 19 out of 21, contrasting with the previous series in which there were only 5 out of 15. All authors of papers on osteoporosis have noted the large predominance of women with this X-ray appearance.

Table II shows also that 9 cases were judged to have a poor diet, deficient in calcium foods and first-class proteins. Of these, 6 were over the age of 65 and of the remaining 3, 1 had had a hysterectomy and had gall-stones, another had had a large partial gastrectomy which was followed by steatorrhœa. Of the 6 over 65 having a poor diet, 3 cases had special diets owing to gastric disorder; the remaining had a deficiency owing either to dislike of certain foods or to financial reasons. In this group over 65 both males are included.

There are 10 cases over the age of 65 and of these 6 were judged to have a poor diet, 4 cases had a good diet and of these 4, one had had a hysterectomy forty years ago and another had been under observation for gastric ulcer and had received medical treatment.

TABLE II.—SPINAL OSTEOPOROSIS

Age	Sex	Diet	Operation	Gastro-intestinal disease
61	F	Good	Hysterectomy	—
63	F	Good	—	—
70	F	Poor	—	—
74	F	Poor	—	—
54	F	Good	Hysterectomy and oophorectomy	—
58	F	Good	Hysterectomy	—
50	F	Good	Artificial menopause	—
68	F	Good	—	Under observation for 3 years gastric ulcer
82	F	Good	Hysterectomy	—
79	M	Poor	Gastro-jejunostomy	Gastric ulcer
67	F	Good	—	"Gastritis"
73	F	Poor	—	"Gastritis"
74	F	Good	—	—
52	F	Good	Hysterectomy	—
65	F	Poor	—	"Gastritis"
66	F	Poor	—	—
46	F	Poor	Hysterectomy	Cholecystitis
54	F	Poor	Partial gastrectomy	Steatorrhœa
48	F	Good	Hysterectomy	—
70	M	Poor	—	—
63	F	Good	Mastectomy (after onset of disease)	—

Thus in this group of cases over the age of 65, dietary deficiency is a prominent factor.

Turning to the 11 cases of 65 and under, it will be seen that 7 had had hysterectomy or artificial menopause performed and their symptoms had started within two years of the operation. This may suggest that osteoporosis is more likely to result after an artificial menopause than after a normal one. Albright and Reifenstein claim that post-menopausal osteoporosis is the commonest of systemic bone dystrophies and that the production of an artificial menopause with the abrupt termination of œstrogenic secretion is more likely to cause this condition than the gradual diminution that occurs during the normal menopause.

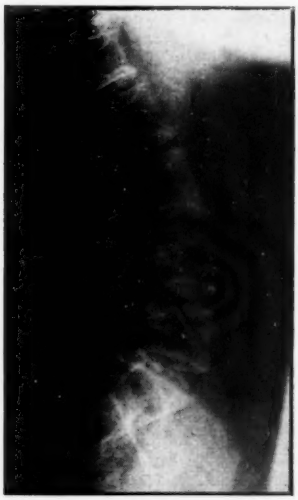

FIG. 5.

Fig. 5, a woman of 66 with a history of a poor diet but no hysterectomy. The photograph shows the general decalcification of the vertebra with the "fishtail" appearance of some; partial collapse can also be seen.

It will be noticed that a defective diet, particularly in first-class protein, is a prominent ætiological factor in the cases over the age of 65. Below that age, I considered that I was studying cases of a post-menopausal syndrome. Illustrating osteoporosis in other conditions were 2 cases where it appeared with ankylosing spondylitis. It may be possible that osteoporosis occurs when there is deficient protein as shown in the aged group or a defect of protein metabolism as demonstrated in the post-menopausal group. Osteoporosis is also found in Cushing's syndrome, where an alteration in the protein metabolism is present, as well as in other disorders of the endocrine glands such as thyrotoxicosis. Finally, in disuse, where there is lack of stimulus to osteoblasts by stresses and muscular action, osteoporosis is common. Therefore, in these cases one might expect a very slow return of normal bone density because there is inactivity of the osteoblasts which is indicated by the low alkaline phosphatase.

Treatment of osteoporosis.—This is directed towards three main objects. Firstly, the alleviation of pain, secondly the prevention of further deformity, thirdly the restoration of the structure of the bones. These aspects of treatment can be carried on simultaneously. The use of œstrogens, the loss of which may be the cause of the osteoporosis, may relieve the pain and also repair the structure. Anderson notes that the administration of natural and synthetic œstrogens gives relief of pain and stiffness in the back but there is no improvement in the radiological findings. Snapper advocates the use of testosterone propionate 25 mg. intramuscularly with the use of œstrogens on alternate days to overcome the masculinizing effects of testosterone.

I have used stilbœstrol and testosterone both independently and together in these cases. In 2 cases I used testosterone propionate 25 mg. on alternate days for two months; in both cases there was a rapid alleviation of symptoms. Testosterone and stilbœstrol used as Snapper advocates were administered in 3 cases for a period of four months. In 2 of these cases where no vertebral collapse could be seen, the response to treatment was very gratifying but in the 1 case where vertebral collapse was present, there was only a partial alleviation of symptoms. In 4 of the cases stilbœstrol 0·5 mg. twice daily was given and in 3 cases again there was a satisfactory alleviation of symptoms, but in 1 case there was only slight improvement. In all cases whether treated with testosterone or stilbœstrol, there was no improvement in the radiological findings. I might add that in the cases where testosterone was used, in 1 of the cases, slight hirsutism occurred.

The endocrine treatment was adopted in the cases aged 65 and under in this series, although in other cases not included, I have used this preparation for patients over that age when I have obtained a history of artificial menopause and there have been radiological findings of osteoporosis.

In order to prevent further collapse or deformity, I have been reluctant to use spinal braces or plaster jackets because of the appearance of osteoporosis when bones are not subject to normal stress.

In the case showing osteoporosis occurring with ankylosing spondylitis (Fig. 4), a disease which has caused a complete splinting of the spine has resulted in osteoporosis. I believe it is probable that if a spinal brace or plaster jacket is worn for a long period in this condition, the mechanism which has caused the osteoporosis may be assisted and although the deformity is prevented, the underlying cause of the deformity has its action enhanced. Therefore I advocate the use of a spinal support only for short periods and only in those cases where relief of pain is not possible by other measures. This view is also taken by Albright. In connexion with the local treatment of the condition I have in all cases employed physical measures such as heat, massage where spasm of the back muscles has been present, and the appropriate exercises for the spine. These exercises do not as a rule increase

the amount of pain except where a considerable collapse of the vertebræ is present. In the cases where collapse is present, then the exercises must be limited to extension exercises only.

The question of short-wave diathermy to this type of case is still a matter for debate. In some experimental work by Hutchison and Burdeaux, they came to the conclusion that short-wave diathermy in repeated clinical doses causes a delay in the union of bone grafts and also a decrease in the formation of osteoporosis, but as the formation of osteoporosis is always associated with increased vascularity and short-wave diathermy will cause increased vascularity on theoretical grounds, I think it would be advisable not to use this type of treatment in osteoporosis. I have used it in certain cases and have noticed a partial alleviation of symptoms due to relaxation of muscle spasm but the symptoms recur as soon as short-wave diathermy has been discontinued. In other cases there has been an actual increase of pain during the administration of short-wave diathermy.

The restoration of the structure of the bones has not been solved as neither the endocrines nor the local treatment appears to have any affect in reducing the degree of osteoporosis. Certainly in cases treated for over six months there has been no evidence as shown by X-ray of any increase in bone. It has been suggested that owing to the gradual onset of the condition it may take a very long time for fresh bone to be laid down in adequate quantities. It may be that with the combination of local treatment and œstrogens, there has been a marked increase in the vascularity around the affected vertebra with the result that one form of treatment has offset another. I am inclined to the view that this condition is irreversible.

Those patients over the age of 65 in whom the osteoporosis may have been due to poor diet, were given extra calcium and vitamin D with local treatment. The local treatment was modified where the general condition was not strong enough, but instead of the spinal supports, exercises to the back were encouraged. With the extra addition of calcium and vitamin D there was a very slow alleviation of symptoms and no improvement in the radiological appearances. It has been suggested that the extra calcium given may be diverted to calcification in the arteries and kidneys, but from X-ray examinations I could detect no increase in the calcification of these structures. With the gradual depletion of calcium over a number of years combined with a less efficient blood supply, there is less likelihood of radiological improvement being observed after a prolonged course of calcium and vitamin D.

Owen and others noted that patients who had senile osteoporosis were capable of retaining increased amounts of calcium but they failed to observe any increase in bone density after an increase of calcium in the diet, in contrast with osteomalacia where the improvement in bone density is very rapid. Calcium and vitamin D by themselves may be insufficient to stimulate the osteoblasts to lay down extra matrix, and the addition of first-class protein is also necessary in senile osteoporosis.

SUMMARY

Osteoporosis is a common problem in our Out-patient Department. Menopausal osteoporosis I have seen more commonly that nutritional osteoporosis and, like Albright, I consider it the commonest of all types of osteoporosis, but in order to arrive at the true diagnosis, it is essential after seeing the X-ray films to exclude all other causes of osteoporosis, particularly multiple myelomatosis. If this disease is not suspected then it is bound to be overlooked; fruitless and even dangerous treatment may be advised. The diagnosis is easy if the disease is suspected. The value of endocrine treatment of menopausal osteoporosis is great particularly if it can be undertaken before the vertebral collapse has occurred. The treatment of nutritional osteoporosis is more disappointing but in both types of condition I believe that spinal supports should only be used as a last resort and that the patient should be encouraged to exercise the back as much as possible in order to prevent the further development of the disease.

[*April* 8, 1953]

DISCUSSION ON THE PRESENT STATE OF PHYSICAL MEDICINE IN THE COUNTRIES OF EUROPE

Group Captain C. J. S. O'Malley: *Physical Medicine and Rehabilitation in Scandinavia.*

(An assessment of this problem as a result of work as Deputy-Director to a Group Training Course on Rehabilitation held in Sweden, Finland and Denmark, October–November 1952)

Sweden

Sweden, the home of remedial gymnastics true to the tradition of Ling, does not have physical medicine specialists as such. The School of Physiotherapy and Remedial Gymnastics is under the control of an orthopædic surgeon at the Karolinska Hospital, Dr. N. Silverskold. Students attend the Physical Medicine Department for approximately three months of their two years' training. This Department is completely separate from the Orthopædic Department where remedial gymnastics

are carried out, and consists of traditional methods of heat, light and electronic therapy. However, an interesting innovation is the work clinic organized by Dr. B. Akerblad in conjunction with Dr. Erland Mindus, an industrial psychiatrist, and the Royal Labour Market Board.

The aim of this clinic is to use work therapy as an aid to assess (*a*) physical work capacity and (*b*) the psychological attitude of the patient towards (i) his work, (ii) his disability and (iii) his associates. This clinic is not part of the hospital and is situated in a separate building, but though geographically separate from the hospital itself it is functionally allied to it. This clinic would appear to act as a bridge between the traditional physiotherapy and occupational therapy departments of the hospital and industry, if the patient can return there, and sheltered workshops if his physical and psychological disability does not allow him to return to a normal working environment. The idea is a good one, but the therapeutic advantage of remedial exercises and remedial games in a balanced programme does not appear to have been appreciated. The scientific work done on work capacity in this clinic is excellent. Dr. Akerblad has been trained as a research physiologist. The weakness of this system is the lack of integration of the various departments—orthopædic, physical medicine and the work clinic—to produce a balanced programme for the patient. Each department appears to work in isolation.

As would be expected, the physiological and kinesiological aspects of motion studies are well appreciated in Sweden, efficient movement and muscle power only being obtained by the constant repetition of the appropriate movements. Movements which are conscious are sometimes subject to inhibitory influences whilst unconscious and instinctive movements such as those performed to music and by remedial games are more often facilitated and efficient. Functional anatomists in Sweden stress the importance of constant repetition by different methods in obtaining efficient function. Stress was laid on the golf swing, the tennis swing, the crawl stroke in swimming, piano-playing, typing, &c. These principles were ably demonstrated in a lecture by Dr. Sjoestrand, Associate Professor of Anatomy of the University of Stockholm.

The impression was formed that individual remedial gymnastics are highly developed but remedial games and group exercises are not much practised. Traditional physiotherapy was made part of a rehabilitation programme but the patient was treated in a separate department working in isolation.

The treatment of the post-concussional syndrome at the Serafimer Hospital by head and neck exercises is similar to that practised at King's College Hospital. The results were uniformly good provided there was a confident approach to a patient, and his domestic and personal problems had been solved by good social work. Occupational therapy followed traditional lines; though some factories had organized sheltered workshops there was nothing comparable to the rehabilitation workshop of Vauxhall Motors.

There is a very large Physical Medicine Department at the Södersjukhuset (2,000 beds) which is the municipal hospital of the City of Stockholm. This Department is very modern with facilities for hydrotherapy, heat, light and electrical treatments, but again the remedial gymnastic side was separate from the physical side and controlled by an orthopædic surgeon.

The Norrbacka Institute situated near the Karolinska Hospital is an efficient institute organized both as an orthopædic clinic, hospital and a cripples' home with the appropriate workshops. This Institute again followed traditional lines, but there were rumours that it would be converted into a modern rehabilitation centre.

Scientific research in Sweden is very highly developed particularly the research into work capacity and occupational health. The application of this scientific research and integration of the various departments was not so well developed but Sweden is fully cognizant of the importance of the integration of all departments concerned in producing a balanced programme of physiotherapy, work therapy and remedial exercises in the rehabilitation of the sick and injured.

Finland

Finland is unique in the fact that the Associations of the Work Disabled have organized their own sheltered workshops and training schools. Remedial gymnastics are controlled by the orthopædic surgeon and there are no physical medicine specialists as such. The most highly organized rehabilitation department was that concerned with the treatment of the brain injured, paraplegics, &c. This system has owed much to the enthusiasm of Professor N. Maki, Professor of Psychology of the University of Helsinki. The best rehabilitation centres we saw in Finland were concerned with these cases.

There is a very large hospital for the medical disorders of the locomotor system, but the rehabilitation side of this problem was not highly developed. However, the teaching of physical medicine and rehabilitation is now being stressed in undergraduate medical education in Finland, and I believe that Finland may very well lead Europe in this work in five years' time.

The sheltered workshops and training schools were highly developed, though the medical control of these workshops appears to be slight. As at the Norbacka Institute in Sweden, the Invalid Foundation, which is an orthopædic hospital and cripples' home is organized on traditional lines, but again there were signs that this institution would be developed into a highly efficient rehabilitation centre. I saw less traditional physical medicine in Finland than in Sweden or Denmark.

Denmark

Physical medicine in Denmark owes much to the enthusiasm and untiring leadership of Dr. Svend Clemmesen of the Municipal Hospital of Copenhagen. His Department though housed in an old building is highly developed and his studies of electromyography are known internationally. In his lecture he stressed the importance of team work and each member of his team gave a demonstration of his own part in the rehabilitation programme, the physiotherapist, the occupational therapist, the social worker and the nurse. Demonstrations were also given of the Bisgaard treatment of varicose ulcers. There was an atmosphere of enthusiasm in this department which epitomized the leadership of one of the pioneers of physical medicine.

There was an epidemic of poliomyelitis raging in Denmark, and a system of treatment and rehabilitation entailing the co-operation between fever hospitals, orthopædic surgeons and physical medicine specialists had been instituted. A large hotel by the sea some 20 miles north of Copenhagen had been taken over as a rehabilitation centre for these cases.

Physical medicine is recognized as a specialty in Denmark, traditional physical medicine being emphasized, though the problems of remedial gymnastics were not so highly appreciated as in Sweden or Finland. Occupational therapy also was organized along traditional lines and the modern concept of equating work therapy with the job to be done in the future was not practised.

The rehabilitation of the blind, the hard of hearing and those suffering from neuroses was practised in separate centres, but as far as one could discover there was no balanced rehabilitation programme organized for post-traumatic cases. There was a highly efficient orthopædic hospital with its allied cripples' home, but this institution was run on traditional lines. Physical medicine is making great progress in Denmark but the integration of physical medicine in a rehabilitation programme has not as yet come to pass.

My impression is that scientific research into the problems of restoration and maintenance of function and the assessment of work capacity is making great strides in Scandinavia, though physical medicine specialists as such are not yet recognized in Sweden or Finland.

Dr. A. C. Boyle (Middlesex Hospital):

My experience is based on a tour of Italy which I carried out in 1952 at the invitation of World Health Organization. The object of this visit was to advise the Italian Government on the setting up of a rehabilitation scheme for handicapped children.

The situation which I found on arrival was both interesting and difficult, and dated back to the immediate post-war days, when all Italy was in social and economic chaos. At that time it was estimated that there were in the whole country some 15,000 children who had been injured to a greater or lesser degree as a result of the war; the vast majority were civilian air-raid casualties, while others had been injured during the actual street fighting. Some of them were indirect and more recent casualties, who had received their injuries by such means as finding and playing with unexploded missiles, or by stepping on undiscovered land mines. To this torrent of war casualties has been added more recently still a trickle of peacetime injuries from street accidents, poliomyelitis and other disabling diseases.

In a country where the gap between riches and poverty is a wide one, and where racial characteristics combine a natural warm-heartedness and love of children, beggary will always flourish, and it soon became clear that many of these children were fast becoming professional beggars, often at the instigation of their parents, for whom they might well provide a satisfactory source of income. The credit for appreciating the plight of these children goes to a priest named Don Gnocchi, who was quick to see that they would never have the benefit either of medical treatment for their disabilities, or of a satisfactory education unless means could be found by which they could be cared for. With the aid, therefore, of radio appeals, street collections and other means, he managed to raise a sum of money with which he formed the Don Gnocchi Foundation, and took over several large buildings in various parts of the country with the object of housing and educating these unfortunate children. At a later date, the Italian Government took an official interest in the Foundation, and is, to-day, partially responsible for financing and administering it.

There are now seven centres—at Rome, Turin, Florence, Salerno, Parma, Pessano, and Inverigo. Four of the Centres are for boys, and two for girls, while the centre at Parma admits both boys and girls. The Centres were at first intended purely as schools for the disabled children, and at each centre the ordinary programme of education is carried out. At a later date, the need for some form of vocational training became obvious, and workshops were set up in some of the Centres where such crafts as tailoring, carpentry, leather work, and pottery are taught, and training can also be given in clerical work and post-office duties. It would seem, however, that there is as yet no formal physical assessment of the children as to their fitness for the particular craft which they are taught, the choice lying largely with the child's especial fancy. The centre at Parma serves a special purpose, in that it is the Hospital Centre of the Foundation, and any children who require further surgical treatment, such as re-amputation, are admitted here for a suitable period. This is the only Centre

which attempts any form of physical treatment, and the physiotherapy is given by one partially sighted medical orderly, who has been trained by the orthopædic surgeons who attend the Centre. It consists only of the simpler types of exercise, but some forms of heat can also be given. A special study has been made at this Centre of reconstructive surgery of the hand, and the function of many of the children with hand injuries has been greatly improved by surgical digitalization of the stump of the amputated thumb. Another feature of the Parma Centre is a workshop where artificial limbs are made on the premises, and some of the older boys are employed on this work, which teaches them a useful craft for future employment.

The Centres in all hold a total of about 1,500 children, ranging from the age of 7 to 19 years, and during my visit I attempted a rough assessment of the types of disability (Table I). In addition,

TABLE I

	Amptn. upper limb	Amptn. lower limb	Monocular blind	Totally blind	Various lesions	Normal	Total
Rome ..	77	13	27	31	52	—	200
Turin ..	210	88	37	—	75	—	410
* Florence ..	15	23	22	—	40	—	100
Salerno ..	41	8	11	—	10	—	70
Parma ..	212	39	35	—	73	—	359
* Pessano ..	48	20	30	2	70	—	170
Inverigo ..	29	9	22	—	65	25	150
Total	632	200	184	33	385	25	1,459

* Centre for girls only.

in order to plan rehabilitation for these children, some assessment had to be made of how many of them had disabilities which were in their final state, and how many might benefit from either reconditioning or from more intensive rehabilitation. Table II shows that approximately 50% of the children could not be considered capable of further improvement.

TABLE II

	Total in centre	Considered static	Need reconditioning only	Need full rehabilitation
Rome	200	112 (56%)	54 (27%)	34 (17%)
Parma	359	212 (59%)	61 (17%)	86 (24%)
Turin	410	184 (45%)	74 (18%)	152 (37%)
Florence	100	43 (43%)	27 (27%)	30 (30%)
Salerno	70	42 (60%)	10 (14%)	18 (26%)
Pessano	170	68 (40%)	37 (22%)	65 (38%)
Inverigo	150	63 (42%)	48 (32%)	39 (26%)
Total	1,459	724 (49%)	311 (22%)	424 (29%)

Although the day-to-day medical care of these children was excellent, a number of them appeared to warrant further investigation, for among the genuine war casualties I saw several cases of old poliomyelitis, in which the paralysis had been ascribed to the late effects of bombing, and there were also what were apparently hysterical paralyses following war incidents. I also saw a case of Still's disease, and another child who was labelled "post-traumatic arthritis" appeared to be a classical case of rickets. Since many of the children had suffered amputation of one or more limbs, it was clearly necessary to make a regular review of the prostheses with which they had been provided, for children very quickly outgrow their appliances. A number of these children had artificial legs which were too small for them, and it was interesting to note that the majority preferred to use sticks or crutches.

From the brief description given, it seems clear that there exists a wonderful opportunity for the employment of a modern scheme of rehabilitation for the benefit of these unfortunate children, and

the question has to be asked whether the present state of physical medicine in Italy is such that this scheme could be provided from resources within the country. For a comprehensive scheme, doctors with a special knowledge of the problems involved, physiotherapists, occupational therapists, and placement officers would be an essential nucleus. There are a few orthopædic surgeons in Italy who are interested in surgical after-care, but on the whole, although operative technique is often brilliant, this essential part of treatment does not arouse very much interest. I visited the Rizzoli Orthopædic Institute, which is one of the most modern orthopædic centres in Italy, but although there is a small physiotherapy department, it is apparently little used for the rehabilitation of patients following surgical procedures. At this Institute there are two orthopædic surgeons who attended a course in the United Kingdom on modern methods of rehabilitation, but although on their return to Italy they wrote a paper on their experiences, their plea for the acceptance of these methods has not met with very great success.

The problem of trained physiotherapists is also a difficult one. Such physiotherapy as is carried out in the centres which I saw, is done by nurses or orderlies who have received some instruction from the doctors for whom they work, but there is no prescribed course of instruction, nor qualifying degree as there is in this country, nor does there seem much prospect of such a training being organized. Most of the special centres train their own physiotherapists, as at the Spolverini Institute at Arricia, which I visited. This Institute is intended for the treatment of children following poliomyelitis, and is provided with gymnasia, and a deep exercise pool. Children are admitted for treatment for as long as may be necessary, and the treatment is carried out by nuns who have had a three to six months' course of training at the Institute. Although I saw a good deal of re-educative exercises being carried out, I gathered the impression that much reliance is still placed on the passage of high-frequency electric currents through the body for the restoration of paralysed muscle.

As with physiotherapy, there is no specific training for occupational therapists, but some hospitals and institutions have personnel who carry out work of a diversional nature.

As in other countries in Europe, a very active programme of aid has been organized for the Don Gnocchi Foundation by World Health Organization and United Nations Invalid Children's Emergency Fund. The latter has provided a full range of physiotherapy and gymnasium equipment for the use of the Foundation, and World Health Organization has allotted two fellowships to Italian doctors to visit the United Kingdom for six months to enable them to take over the rehabilitation scheme on return. A member of our own British Association of Physical Medicine is shortly leaving for Italy to initiate the scheme, and to commence training Italian Red Cross nurses in basic physiotherapeutic techniques. It is to be hoped that the Centre at Rome may act as a model for future rehabilitation schemes, and that a permanent training school for physiotherapists will eventually be established there.

No paper dealing with the rehabilitation of the disabled in the countries of Europe would be complete without referring to the work of the late Dr. H. Balme, by whose personal efforts much of what I have described has been achieved. Although a sick man, he did not spare himself during the last years of his life in his efforts to alleviate the distress of his fellow men. The Centre at Rome will remain one of many fitting tributes to his memory.

[*May* 16, 1953]

MEETING HELD AT COURTLANDS HOSPITAL, WEST WORTHING, SUSSEX

Intractable Œdema of the Leg [*Abstract*]

By CHARLES L. HEANLEY, F.R.C.S., M.R.C.P.

THERE are many causes of œdema of the leg and often the swelling is due to several concomitant causes. In all cases we must bear in mind œdema brought about by systemic disease: heart failure, renal disease, malnutrition of the tissues due to anæmias, and dietetic causes. In women swelling of the limbs, from whatever cause, is often aggravated in the premenstrual phase and can be treated by anti-œstrin substances and diuretics. There is no doubt that the swollen limb occurs more frequently in the female than the male, and we realize that this may be due to hormonal as well as anatomical influences.

The swollen limb in relation to diseases of the vessels.—Œdema in arterial disease is serious and should be treated by immediate rest in bed; the limb being elevated to a level at which it is neither congested nor white. This position is often painful and must be treated by ample sedatives; the desire of the patient to hang the leg down in the most comfortable position is not to be encouraged. Pain

at rest is symptomatic of occlusion in the smaller arteries whereas pain on movement, so-called claudication, is indicative of blocking of the larger arteries. If, with rest, the œdema disappears, sympathectomy is often beneficial. If œdema persists, sympathectomy is often harmful and high amputation is usually required.

Venous occlusion of the leg leads to swelling, and is seen most commonly in the all too frequent post-decubitus swollen leg. The hydrostatics of the venous system are often misunderstood. When the person stands immobile the venous pressure in the dependent part is exactly the same, whether or no efficient valves are present; the blood accumulates in the distal veins and only when the muscles move do the valves come into their own. The soldier standing still on parade faints as his blood accumulates in his legs, and such fainting can easily be prevented by a little surreptitious quadriceps drill, provided his veins have valves! The advice to a patient should be: never sit when you can lie, never sit with your legs dependent—and have a soft edge to your chair, never stand when you can sit, and never stand still. The other important function of the valves is to prevent back pressure from sudden rises of intra-abdominal and intrathoracic pressure due to straining or coughing. Classically the highest valve is just above the saphenous opening; often it is absent and the highest valves are at the saphenous opening and the femoral vein. Venous thrombosis leads to œdema of the leg.

Thrombosis has many causes: (1) changes in the coagulability of the blood; (2) sluggishness of the circulation due to immobility in bed—here physiotherapy is of immense help, e.g. extension and flexion of the ankle-joint increases greatly the venous return from the leg; (3) infection leading to thrombophlebitis—usually due to the *B. coli*. In the old days potassium citrate was used, but nowadays we can use the specific antibiotics against *B. coli*. The association of thrombophlebitis with ulcerating carcinomas of the gut is well known, and it is also associated with *B. coli* infections of the kidney.

The patient in bed develops a deep venous thrombosis, and when early ambulant, the limb swells. After a time the other veins take over the venous return and for a time all is well and may remain so; in others, especially the younger woman—as with a post-puerperal deep thrombosis—the vein recanalizes, but without valves, and the leg swells again and the patient complains of bursting pain. Treatment here is ligation of the deep vein in the popliteal fossa. Thrombosis in the superficial veins seldom causes persistant œdema, as other veins take over their function. In this connexion the posterior veins over the buttock are important.

Lymphatic obstruction is undoubtedly the cause of the most severe swellings of the leg. In this country the pure, uncomplicated lymphatic obstruction is rare. In filarial districts it is all too common. In Cochin, India, I made a count, and one in five people seen in the streets suffers from gross swelling of one or both legs. The accumulation of lymph in the tissues leads to infection, and this to fibrosis, and this in turn to increased obstruction, and so a vicious circle results; the limb becomes massive and a true irreversible elephantiasis results. The only possible treatment is to remove all tissues superficial to the deep fascia, and re-epithelialize the limb by skin grafting. In early lymphatic obstruction where there is pooling of the lymph, with little or no fibrous reaction, help may be obtained by turning the lymphatics from the lower abdominal wall into the leg, by excision of scar tissues, and, in the case of the arm after radical mastectomy operations, by burying skin strips. Kondoleon's operation is not a successful one.

Usually swelling of the leg is brought about by a combination of venous and lymphatic obstruction: varicose veins lead to ulceration from malnutrition of the skin; thus a portal of entry is formed for infection which leads to fibrosis and thus to lymphatic obstruction, and so the vicious circle of repeated lymphangitis starts. It is important to secure early healing in the varicose ulcer, and proper treatment of all skin sepsis, especially that of tinea. Rest and elevation and the use of the two-way-stretch bandage are also important as is the immediate use of specific drugs at the slightest sign of lymphangitis.

Perthes' test helps in deciding upon surgical treatment of veins—a rubber band is applied round the leg sufficient to obstruct the superficial veins, then the patient is instructed to walk round the room. If there are superficial varicose veins and these collapse, it is indicative that the deep vein is patent with efficient valves, and then ligation of the superficial veins or their excision is indicated and ulceration and localized swelling will be helped. If the superficial veins dilate, which is often very painful, it means that the deep vein is thrombosed, and ligature of superficial veins is unwise. If there is no change it means that the deep vein is patent but incompetent, and ligature of the deep vein may be wise.

In brief, the commonest cause in this country of intractable œdema of the leg is initially a deep venous thrombosis. This venous obstruction causes an initial increase of lymph in the tissues, and it is infection of this lymphatic pool that leads to fibrosis, and increased lymphatic obstruction, more pooling, more infection, and so the vicious circle progresses. The physiotherapist, by increasing the rate of venous circulation in the recumbent patient, prevents deep thrombosis, and thus the occurrence of post-decubitus swollen leg. The patient who has to lie in bed should be told that it is best not to lie still.

Rheumatoid Arthritis from the Point of View of a General Physician

By W. A. Bourne, M.D.

The subject of rheumatoid arthritis interests me, for one reason, because I have had an attack of it and because of it I have given up golf and sailing. For another reason, because twenty-five years ago I wrote an M.D. thesis on urinary proteose in rheumatoid arthritis, with the usual negative results.

As a general physician when I compare the cases I see now with those I saw in 1938, organic nervous diseases are only 40% of what they were, respiratory diseases 37%, and cardiac disease is only 70%. These diminutions are mainly due to establishment of new units or increased activity of old. On the other hand, digestive diseases have risen from 16% to 25%, and rheumatic diseases from 16% to 24%.

During about eighteen months in 1951–2 I saw 3,458 new patients at Hospital and privately. 24% or 828 were seen for rheumatic conditions, of which 128 were diagnosed as rheumatoid arthritis. This is almost the same as the proportion of hypertension, rather less than proved peptic ulcer, and rather more than obesity. The figures for hospital and private patients were practically the same. A considerable number were long-standing cases, and at the other end of the scale, early cases are, I think, difficult to diagnose confidently.

For in-patients, in acute medical beds the proportion is the same. At the Royal Sussex County Hospital the percentage of medical admissions for rheumatoid arthritis was 2½% in 1950, 2% in 1951, and 3% (31 of 1,051) in 1952.

In the Brighton General Hospital, with 290 geriatric and long-stay beds, the proportion of rheumatoid cases in what are called the acute geriatric beds is 7·5%, and in the chronic wards 33%.

These latter figures seem remarkably high, and it is helpful to remember the findings of Kellgren and others in Leigh (1953), and Jacobs (1953) in Cambridgeshire. In both areas the complaints attributed to rheumatoid arthritis formed about 2% or 3% of the whole, so that the medical out-patient population with which I deal is not very different from the general population. This figure of 3% was found also by Sheldon (1948) in his work on the social medicine of old age in Wolverhampton. He pointed out, however, that the incidence of incapacity steadily increased with the age of the patient, almost certainly due to chronic overworking of a diseased joint, the effects of which increase as the years go by. The figures from the Brighton General Hospital are in accordance with this. A non-killing disease like rheumatoid arthritis thus represents a heavy liability in terms of future bed-requirements in geriatric units.

Diagnosis of rheumatoid arthritis forms part of the diagnosis of pain, swelling, stiffness and deformity. In general I think of such symptoms and signs as being either biochemical or mechanical in origin. I have, however, seen them produced by quite different and generalized disease. Degenerative joint lesions and gout are my first two alternatives, and I have 40 cases of gout in my present series. I have, however, suspected rheumatoid arthritis in leukæmia, dermatomyositis, xanthomatosis, acromegaly, all of which can give pain and swelling. Stiffness can be produced by scleroderma, by nervous disease such as Parkinsonism, or unrecognized hemiplegia, or by the shoulder-hand syndrome following coronary artery disease. Acute rheumatism does not concern us in this context, but there is a form of rheumatoid arthritis of very sudden onset, often with fever, accompanied by very marked œdema of the hands, which I have been tempted to call rheumatoid fever. One such case was referred to me by a surgeon who suspected bilateral axillary vein obstruction: another case had pleural effusion. The course of these cases shows them to be rheumatoid, but there is the strongest indication of general disease.

Occasionally such general disorder is the presenting feature. Anæmia, lymph-node enlargement and wasting were present in 2 cases for some years before characteristic rheumatoid joint changes appeared, and in Felty's syndrome joint lesions were the last feature to develop. A similar instance was that of a patient with unexplained granulocytopenia, who was at last found to be developing rheumatoid arthritis.

There is not, at present, I think, any certain accessory means of diagnosis except biopsy. Judged by the standards of general medicine, no biochemical or immunological test gives much more than a 70% or 80% probability: it is merely a pointer to diagnosis. In this problem of diagnosis we encounter what the physicists call the principle of indeterminacy. There are such a number of lines of approach that I feel there may well be a number of defects in bodily metabolism and resistance, any one of which may cause a breakdown in the small joints in particular, so that there may be as many causes of rheumatoid arthritis as there are of clubbing of the fingers, and we ought to speak of the rheumatoid arthritis syndrome.

The question of diagnosis does not confine itself to the small joints. Soft tissues, particularly muscles, may be affected, and I would think the shoulder girdle muscles not uncommonly show symptoms, particularly the "jelling" phenomenon (symptoms and dysfunction are made worse by rest or cool environment, worse on arising, and better from mid-day until evening. *See* Committee of American Rheumatism Association, 1949). In such cases, relaxation rather than physiotherapy is indicated.

The lymphoid lesions often associated with the Felty syndrome have been mentioned. Pulmonary lesions have been suspected in a number of cases, but the recent reports by Fletcher (1953) and others on the very characteristic types of change seen in pneumoconiosis associated with rheumatoid arthritis suggest either that there is more than one sort of lesion, or that some appearances are non-specific and that we shall have to be stricter in our criteria. It is curious that pulmonary lesions (neoplasm) can apparently cause rheumatoid arthritis without notable pulmonary lesion of the rheumatoid type.

The concept thus arising is of a diffuse process with a local manifestation, the causes being obscure, and the complex being describable essentially in terms of clinical and histological abnormality to which no clear endocrinological or biochemical date can be attached.

Treatment, at best, is only empirical.

In such assessments it is worth remembering the statement of Louis Rénon (1914) in respect of pulmonary tuberculosis that "a comparison of the results obtained by the various methods of anti-tubercular treatment shows that these results are practically identical in all cases, the percentage of cases cured or alleviated ranging from 65% to 71%. I have described this proportion", said Rénon, "as 'the normal coefficient of amelioration'. The particular medication is no more than the vehicle of suggestion."

Past treatment of rheumatoid arthritis provides an example of this. Far too commonly patients say of a doctor "He helped me a lot—I went to him for two years." Five years ago I found 13% of my rheumatic patients had attended for more than six months. Compared with any disease for which we have a true cure, these statements indicate no cure. It must be remembered, also, that many patients never consult a doctor—in Leigh 20% of males and 40% of females—and yet do, one presumes, reasonably well. The disease, in other words, limits itself, and notoriously may do the same under treatment. I doubt if any condition shows more depressing instances of self-deception on the part of a practitioner. To quote one example only of treatment, namely aurotherapy, which is, I think, under scrutiny in a number of centres: In Hove we have had 40 cases under treatment for two years, half having gold and half control injections. Only one individual in the hospital—the pharmacist—knew the substance injected in each case. No evidence has been obtained that gold was of more benefit than the control, though I would not say it was of no benefit. "No placebo has no effect". It is interesting to note the attitude of the medical observer: two courses of the control were interrupted because a gold dermatitis was suspected. Such is one difficulty in a consistently conducted control series.

Cortisone and ACTH give very much more definite results, but even here somewhat similar difficulties arise. A recent full review by Thorn and others (1953) indicates that in the vast majority of cases the administration of adequate suppressive doses results in a marked improvement in the patients' general condition. It is clear, however, that there are differences in opinion as to the best means of treatment and a general agreement that there are many factors poorly understood or quite unknown. A general physician would say, I think, that this also is at present an empirical but often valuable method of relieving a disease for which at present there is no cure. Discovery of a cure depends very largely on a knowledge of the cause.

In considering the cause I myself think very largely in terms of function and have little use for the concept that rheumatoid arthritis is a mesenchymal disease except by accident. I am accustomed to say that the human body is the only means by which the human personality can adapt itself to and express itself upon its environment. As a result, any conflict between personality and environment, or difficulty in adaptation and expression, is likely to involve some degree of somatic change. We are familiar with psychosomatic disease of stomach, bowel, skin and circulation. I feel that rheumatoid arthritis is often a psychosomatic disease of the locomotor system, and, since we move about in our environment by means of our mesenchyme, from which were formed our muscles, bones and joints, rheumatoid arthritis is labelled mesenchymal—but only, as I say, by accident.

Of course, no evidence has been found by the Empire Rheumatism Council (1950) that rheumatoid arthritis patients have undue psychogenic factors. It is, however, my experience that in a number of diseases where, to any ordinary observer, there seem adequate causes, the patient has often denied any emotional stress, and I think rightly. It seems to me that the emotional motors driving our personalities are geared partly through our cortexes and partly through our vegetative centres and I believe it quite possible that the drive to the cortex can be cut out and the drive to the vegetative centres thereby stepped up. These patients say they do not worry, and I do not believe they do, but there is a turmoil in their hypothalamus or thereabouts, transferred somatically.

How, on this basis, would I explain rheumatoid arthritis? It is essentially a lesion of small joints, especially the hands. It is not due to a general lowering of joint resistance to normal stress, or why do not other joints break down? There is indeed, I would say, following Kellgren and Moore (1952), a different disease where lowered joint resistance is the primary factor, so that changes in interphalangeal joints can indicate lumbosacral disease. This is, however, exceptional in rheumatoid arthritis. The alternative explanation is undue stress in the joints. One might expect the hands to be affected by cortical activity, for the human hand is a very important anthropological phenomenon, which has

even been suggested as reponsible for part of that cortical overgrowth which demarcated man from the rest of the brute creation. Emotional turmoil may easily express itself in unconscious muscle activity in the hands, and we are familiar with clenched fists, writhing fingers, and so on.

We should remember also that not only is the human hand the most delicate physical instrument the world has known, but it can be put to enormous stress. The small joints and intrinsic muscles have to take all the oarsman's drive of leg and back muscles, or thrash a golf ball two hundred yards, or take many other severe, violent or sudden strains. Such demands may often be made by an obsessional temperament on these small structures. Women shopping, for example, manipulate heavy bags with overladen fingers repeatedly and rapidly. If chemical processes not at present understood are defective, this physical strain which we do understand can determine that form of breakdown we call rheumatoid arthritis.

The conception of rest by avoidance of voluntary movement has been familiar since the days of Hilton. I believe, however that there is another source of strain, unconscious muscle tension, producing what may be called defective manual posture. Barlow (1952) has written on postural homœostasis, and the therapeutic approach arising therefrom, and I believe it can be applied equally to the hand.

That postural defect can produce joint damage is most easily demonstrable in the vertebræ. It is sometimes possible to diagnose right or left-handedness from a lumbo-sacro-iliac X-ray; a lifelong postural defect will produce spinal arthritic changes strikingly demonstrable on the X-ray film, but the backache comes from the posture and not from the osteophyte.

In the same sort of way, manual posture and functional defect may predispose to rheumatoid arthritis, and I cannot help feeling it would be worth trying relaxation of forearm and hand muscles as a part of treatment. This problem has been approached by a psychiatrist, Garmany (1952), for his own purposes, and he remarks that "there is no doubt at all that it is most unwise to go further" until . . . "the hands and forearms have been patiently treated until reasonably good relaxation is obtained". It is interesting that Barlow finds physical medicine leads to personality change and Garmany finds personality problems helped by physical medicine. I am probably biased in this matter, since I have myself rheumatoid arthritis, and I am conscious that I have a habit of tightening my hand muscles, pointed out to me years ago by a golf professional. It is, however, a habit common to many tense individuals.

I do not believe that the biochemical and materialistic approach to the problem of rheumatoid arthritis will suffice, and indeed that is the lesson of cortisone. The patient must be regarded as a whole, but one of the most important parts is, I believe, that with which physical medicine is concerned. In general medicine we have been in the habit of thinking in terms of organ inferiority: but nowadays we are less anatomists than physiologists, and our diagnoses are not so much in terms of deformity of structure as of defect of function. Cortisone may remedy the structure but not the function, that co-ordinated use of body and limbs which is the particular sphere of physical medicine, emphasized lately by Lovatt Evans (1953).

Rheumatology is full of facts which are not understood. The constitutions of the ketosteroids, for instance, are set out with the precision of hands at bridge, but at present we can say no more of what they really do than we can foretell how the cards will be played. To quote Aristotle: "It is an easy matter to know honey, wine, hellebore, cautery or the use of the knife, but the knowing how one should administer these with a view to health, and to whom and at what time amounts in fact to being a physician."

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